NORTH CAROLINA Medical Journal

Vol. 20 No.12
December, 1959

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THE PRACTICE OF TUBAL LIGATION IN NORTH CAROLINA
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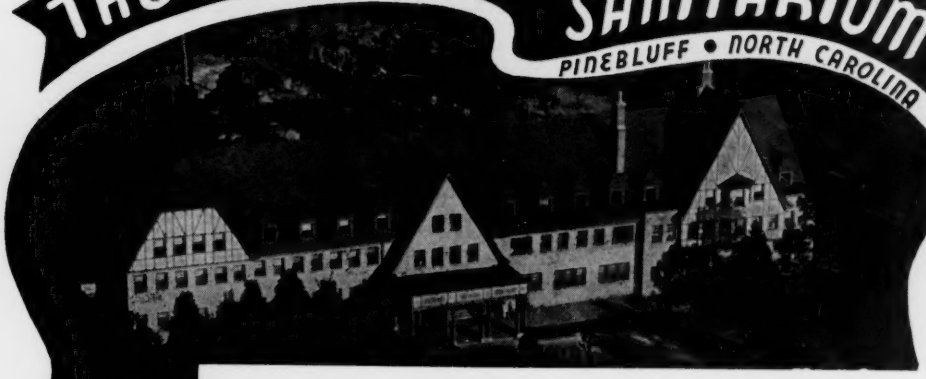

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VOLUME 20
NUMBER 12

DECEMBER, 1959

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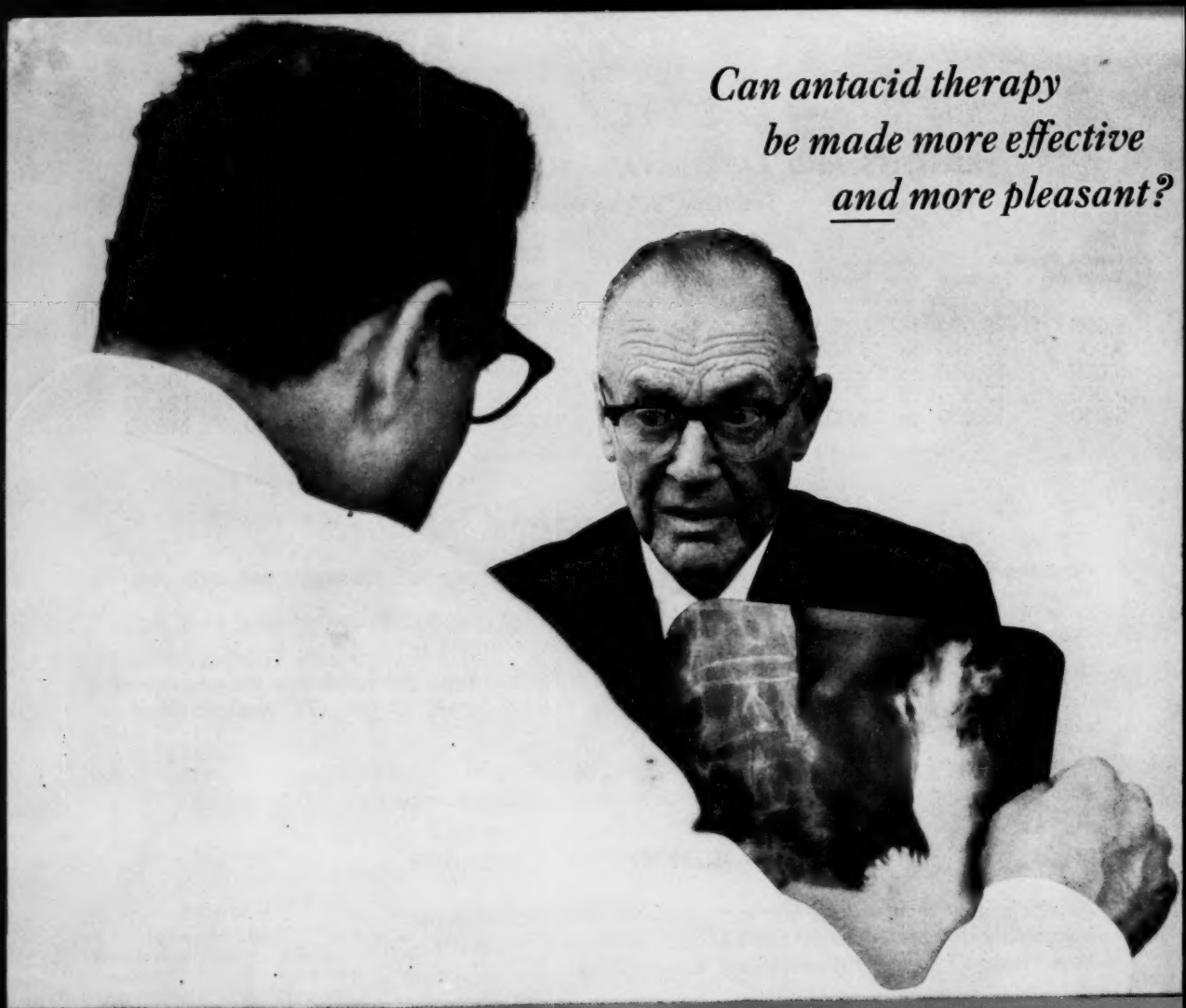

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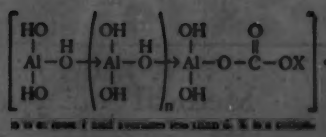

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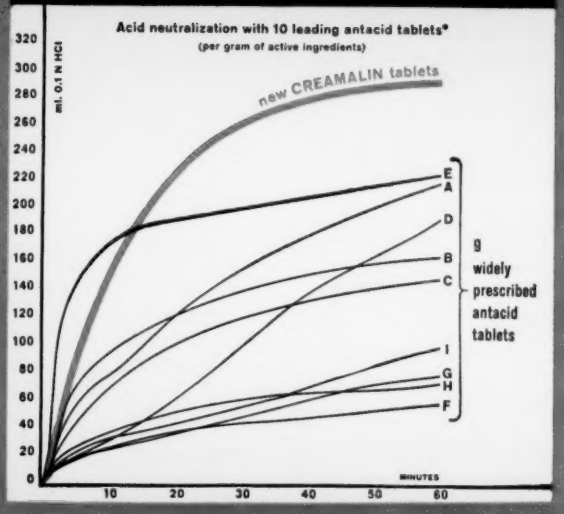

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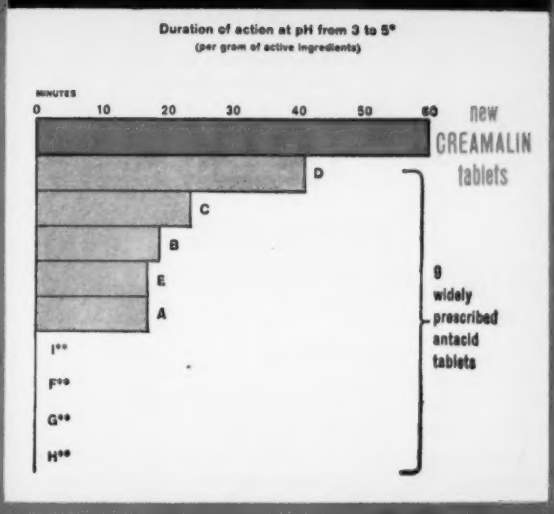

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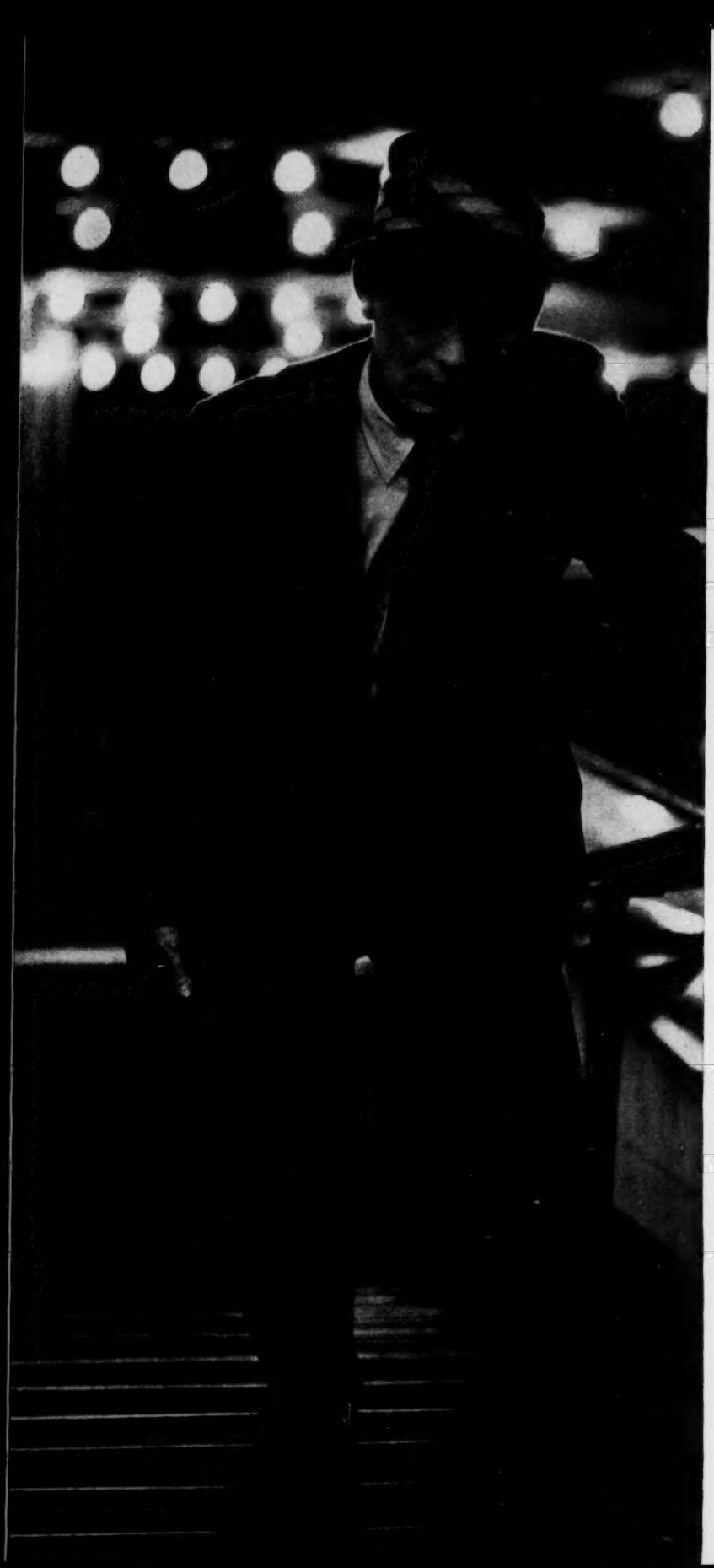

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(1) Beck, J. W.; Saavedra, D.; Antell, G. J., & Tejeiro, B.: Am. J. Trop. Med. 8:349, 1959.

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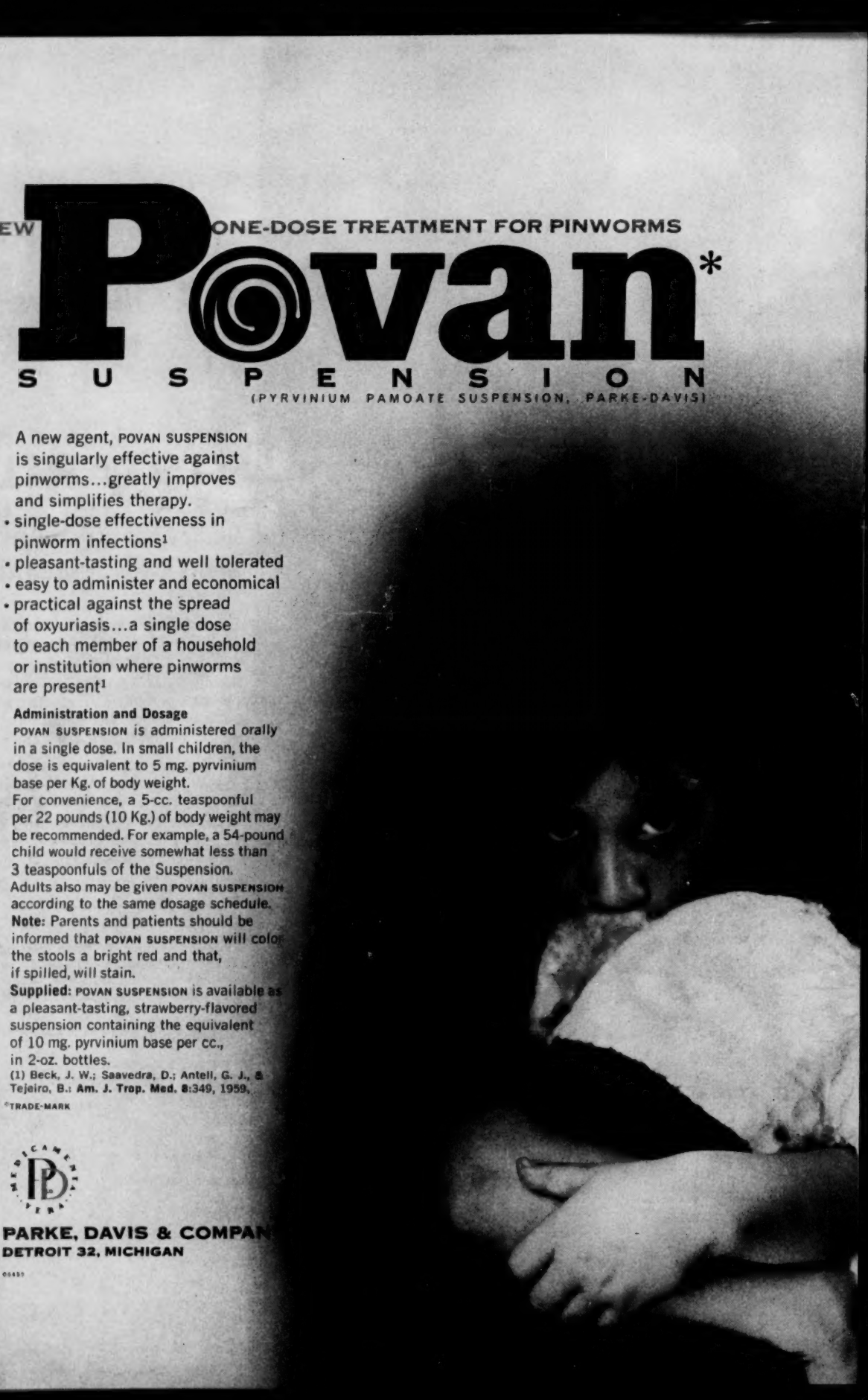

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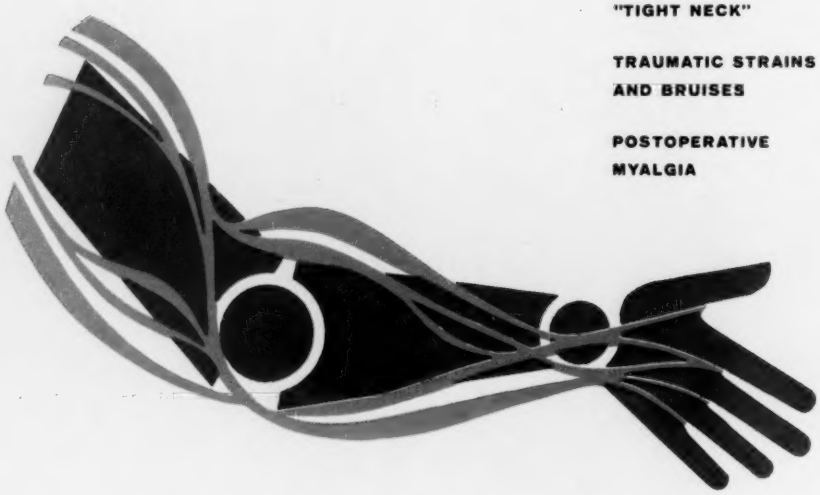

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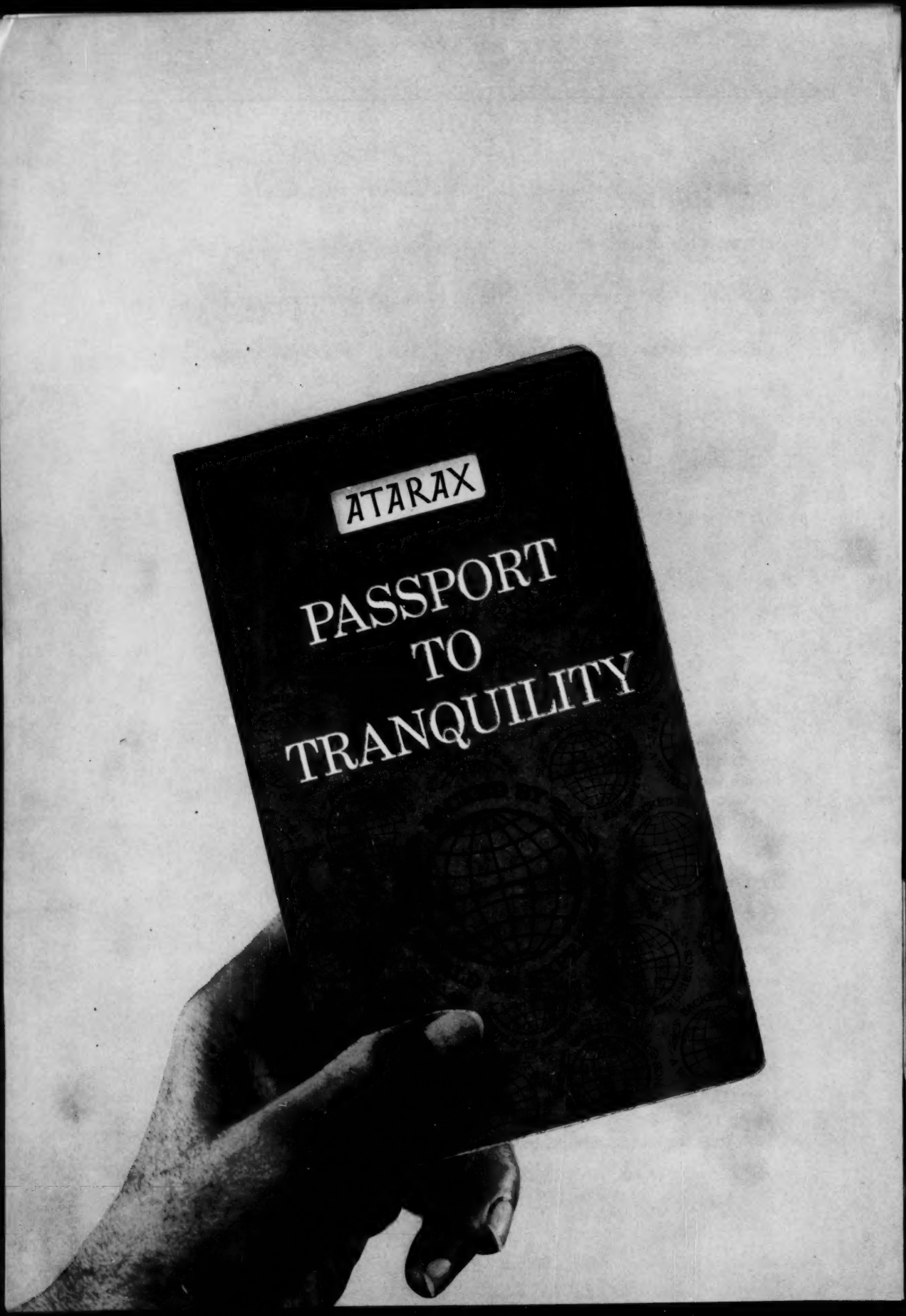
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References: 1. Farah, L.: Internat. Rec. Med. *169*:379 (June) 1956. 2. Smigel, J. O., et al.: J. Am. Geriatrics Soc. *7*:61 (Jan.) 1959. 3. Feinberg, A. R., et al.: J. Allergy *29*:358 (July) 1958. 4. Eisenberg, B. C.: J.A.M.A. *169*:14 (Jan. 3) 1959. 5. Maryssael, L.: Bruxelles-méd. *38*:141 (Jan. 26) 1958. 6. Pfleger, R.: Med. Klin. *53*:1030 (June 5) 1958. 7. Over 200 laboratory and clinical papers from 14 countries.

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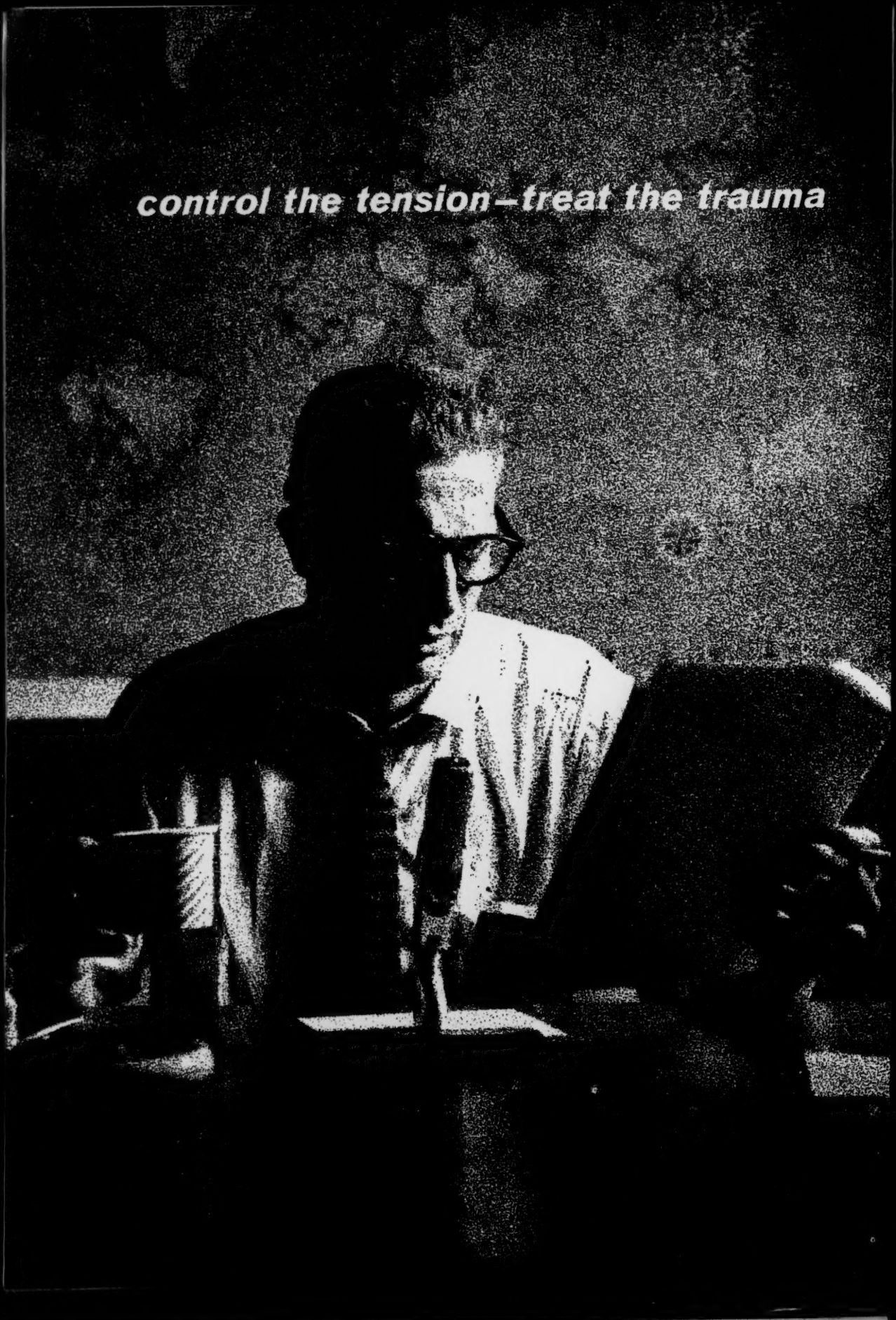
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meprobamate with PATHILON® tridihexethyl chloride Lederle

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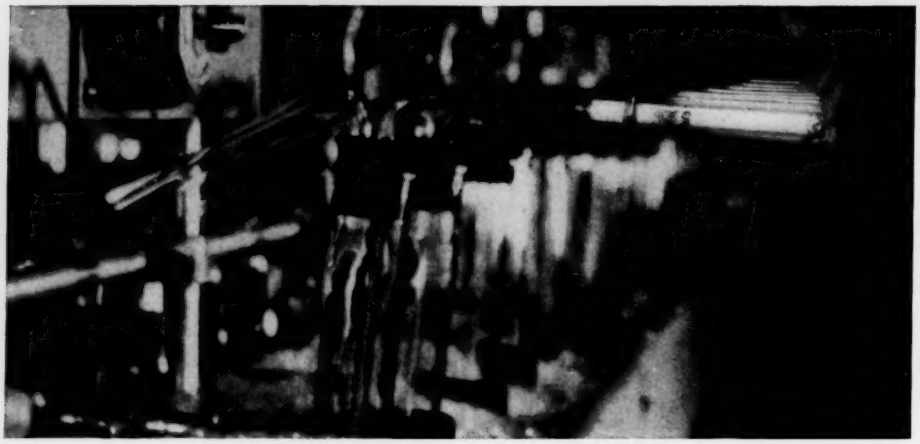
Administration and Dosage: PATHIBAMATE-400—1 tablet three times a day at mealtime and 2 tablets at bedtime.
PATHIBAMATE-200—1 or 2 tablets three times a day at mealtime and 2 tablets at bedtime.
Adjust to patient response.

Contraindications: glaucoma; pyloric obstruction, and obstruction of the urinary bladder neck.

Lederle

LEDERLE LABORATORIES, A Division of AMERICAN CYANAMID COMPANY, Pearl River, New York

HOW KENT BLAZED THE TRAIL TO LOW TAR AND NICOTINE CONTENT



A major independent research foundation, under Lorillard sponsorship, determined that the average puff of cigarette smoke contains over 12 billion semi-solid particles. Further research revealed that inhaled smoke from ordinary cigarettes has a predominant proportion of particles, from 0.1 to 1 micron in diameter, averaging 0.6 micron.

Ordinary filter fibers are so large that they create spaces through which the small semi-solid smoke particle can easily pass. However, in the extraordinary Kent filter, the fibers are mechanically manipulated in such a manner as to create a multitude of baffles and extremely tortuous passageways for the smoke. This is the "Micronite" Filter.

Lorillard pioneered research into filtration—creating a filter of extraordinary ability to decrease smoke solids. So—from the very start—Kent blazed the trail to the lowest level of tars and nicotine among all leading brands. And today, tars and nicotine are at the lowest level in Kent's history.

This Kent achievement in the field of filtration was done without sacrifice of rich tobacco flavor. Kent uses only 100% natural tobaccos—the finest in the world today—to give you real tobacco taste. Kent satisfies your appetite for a real good smoke.

If you would like the booklet, for your own use, "The Story of Kent," write to: P. Lorillard Company, Research Department, 200 East 42nd Street, New York 17, N. Y.

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KENT FILTERS BEST
for the flavor you like

A Product of P. Lorillard Company—First with the finest cigarettes—through Lorillard Research!

in peptic ulcer

Results with "... antacid therapy with DAA are essentially the same as ... with potent anticholinergic drugs."

Alglyn®

Dihydroxy aluminum aminoacetate, N.N.R.

In recent years, a number of new synthetic anticholinergic drugs with numerous and varying side effects have been investigated for treatment of peptic ulcer. However, a double-blind study conducted recently by Cayer et al suggests that the use of such anticholinergic drugs is seldom necessary. The authors concluded that "The percentage of 'good to excellent' results obtained in patients on continuous long-term antacid therapy with DAA (74%) is essentially the same as that previously noted in ulcer patients treated under similar conditions with potent anticholinergic drugs alone."

The authors' choice of dihydroxy aluminum aminoacetate (DAA) was based on the fact that "the tablet form of DAA (is) more active than a variety of straight aluminum hydroxide magmas." They further commented that "Because of the convenience of tablet medication as compared with the liquid gel—a convenience which in the use of other tablets is gained at the expense of therapeutic effectiveness—dihydroxy aluminum aminoacetate was used exclusively."

ALGLYN (dihydroxy aluminum aminoacetate) Tablets are supplied in bottles of 100 tablets (0.5 Gm. per tablet).

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QUESTIONS ON THE CLINICAL USE OF KANTREX

Q Why should I use KANTREX® Injection* when there are so many other antibiotics available?

A

Because KANTREX Injection is bactericidal to a wide variety of organisms, including many that are highly resistant to the other antibiotics[3,4,10,12,13,17,18,20,21,23,24,25,27,30,33,35,37]

—organisms such as *Staph. aureus, Staph. albus, A. aerogenes, E. coli, H. pertussis, K. pneumoniae, Neisseria* sp., *Shigella, Salmonella* and many strains of *B. proteus.*

Q *But if I use* KANTREX *Injection, won't that help make bacteria resistant to it also?*

Next page, please .....

* Kanamycin sulfate injection (Bristol)

Q *But if I use* KANTREX *Injection, won't that help make bacteria resistant to it also?*

A A very good question, but it is reassuring to note that in almost two years of clinical use of KANTREX for the treatment of infections for which it is recommended, the emergence of KANTREX-resistant bacterial populations has not been a problem.

Q *My impression is that* KANTREX *is just another neomycin. Isn't that so?*

A Indeed not. The only thing KANTREX and neomycin have in common is a similar antimicrobial spectrum. Otherwise, they're very different: they have different chemical structures; the toxicity of KANTREX is "much less than that of neomycin"[14]; and clinically, KANTREX Injection is practical for systemic administration routinely, while neomycin is not.

Q *You mean that* KANTREX *Injection doesn't have the nephrotoxicity of neomycin?*

A Precisely. It's true that when KANTREX Injection is used, urinary casts – even slight albuminuria or microscopic hematuria – may appear, especially in poorly hydrated patients, but this does not reflect any progressive damage to the kidneys. These signs promptly disappear on adequate hydration or termination of therapy.

Q *Then why do you recommend reduced dosage in patients with renal impairment?*

A Because renal impairment causes an excessive accumulation of KANTREX in the blood and tissues, when usual doses are administered. Since KANTREX Injection is excreted entirely by the kidneys, renal impairment leads

to unnecessarily high and prolonged blood levels; and such excessive concentrations increase the risk of ototoxicity.

Q *Is that why we see reports of patients developing hearing loss during* KANTREX *Injection therapy?*

A Yes. A study of the few reported cases in which patients have suffered impaired hearing will show that in every instance they had pre-existing or concurrent renal impairment, yet received usual or excessive doses of KANTREX Injection. Dosage recommendations for KANTREX Injection emphasize that in patients with renal dysfunction, adequate serum levels can be achieved with a fraction of the dose suggested for patients with normal kidney function – with minimal risk of ototoxicity.

Q *Since urinary tract infections are often accompanied by renal impairment, does that mean I shouldn't use* KANTREX *Injection in such conditions?*

A Not at all. With proper precautions, KANTREX Injection is an excellent drug for the treatment of urinary tract infections, especially those due to *Proteus, A. aerogenes* and *E. coli,* even when renal impairment is present.

Q *What are the "proper precautions" in a patient with impaired renal function?*

A The package literature covers them in detail. First, the daily dose should be reduced in such a patient. Then, if he is going to receive KANTREX Injection for 7 days or more, a pre-treatment audiogram should be done, and it should be repeated at appropriate intervals during therapy. If tinnitus or subjective hearing loss develops, or if followup audiograms show significant loss of high frequency response, KANTREX therapy should be discontinued. However, therapy for 7 days or more

is seldom required because the clinical response to KANTREX Injection is so rapid.

Q *Why do you put so much emphasis on* KANTREX'S *"rapid action"? Every antibiotic I've heard about is supposed to be "rapid acting."*

A There is such an abundance of clinical evidence about "rapid acting" that it takes KANTREX Injection out of the "supposed-to" class.[1,2,3,7,8,9,11,15,16,19,21,22,26,29,32,33] Remember, the effectiveness of KANTREX Injection therapy can usually be appraised in 24 to 36 hours. That's definite evidence of rapid action. In fact, one group of investigators reported that "the rapidity with which bacteria are killed by this agent is reflected by the promptness of the clinical response."[29]

Q *Does* KANTREX *Injection cause blood dyscrasias?*

A In extensive clinical and toxicity studies by numerous investigators, as well as almost two years of general use, not a single instance of such toxicity has been reported.

Q *Can I administer* KANTREX *Injection in any other way than by the intramuscular route?*

A Yes. While it's usually given intramuscularly, other routes are practicable: intravenous, intraperitoneal, by aerosol, and as an irrigating solution. Complete instructions are included in the package insert.

Q *So you think I ought to use* KANTREX *Injection as my first choice antibiotic in staph and gram-negative infections?*

A Yes – because all evidence to date indicates that it is bactericidal against a wide range of organisms...rapid acting...does not encourage development of bacterial resistance...is well tolerated in specified dosage...and has not caused any blood dyscrasias.

KANTREX® CAPSULES

for local gastrointestinal therapy... not for systemic infections

Q *Why can't I use* KANTREX *Capsules for systemic medication?*

A Because there is only negligible absorption of KANTREX from the gastrointestinal tract.[3,5,6,8,28,34] Thus, capsules cannot provide effective blood levels.

Q *Then what are* KANTREX *Capsules used for?*

A Preoperative bowel sterilization, and local treatment of intestinal infections due to kanamycin-sensitive organisms.

Q *I've been using neomycin for preoperative bowel sterilization. Why should I switch to* KANTREX *Capsules?*

A Because KANTREX has been rated as "superior to neomycin" for this purpose.[6] It provides rapid and satisfactory control of coliforms, clostridia, staphylococci and streptococci; yeasts do not proliferate; stool concentrations of the drug are exceptionally high; and nausea, vomiting or intestinal irritation have not been observed.[5,6]

Q *What advantages do* KANTREX *Capsules offer me in the treatment of intestinal infections?*

A A high degree of effectiveness against most of the pathogens responsible for such infections: *Salmonella, Shigella, Staph. aureus, E. coli* and *Endamoeba histolytica.* Moreover, their use has been "remarkably free of any side effects."[31]

KANTREX®

INJECTION KANAMYCIN SULFATE INJECTION

INDICATIONS

Infections due to kanamycin-sensitive organisms, particularly staph or "gram-negatives": genito-urinary infections; skin, soft tissue and post-surgical infections; respiratory tract infections; septicemia and bacteremia; osteomyelitis and periostitis.

DOSAGE: INTRAMUSCULAR ROUTE

Recommended daily dose is 15 mg. per kg. of body weight, in 2 to 4 divided doses.

For intramuscular administration, KANTREX Injection should be injected deeply into the upper outer quadrant of the gluteal muscle.

TOXICITY

When the recommended precautions are followed, the incidence of toxic reactions to KANTREX is low. In well hydrated patients under 45 years of age with normal kidney function, receiving a total dose of 20 Gm. or less of KANTREX, the risk of ototoxic reactions is negligible.

In patients with renal disease and impaired renal function, the daily dose of KANTREX should be reduced in proportion to the degree of impairment to avoid accumulation of the drug in serum and tissues, thus minimizing the possibility of ototoxicity. In such patients, if therapy is expected to last 7 days or more, audiograms should be obtained prior to and during treatment. KANTREX therapy should be stopped if tinnitus or subjective hearing loss develops, or if audiograms show significant loss of high frequency response.

OTHER ROUTES OF ADMINISTRATION

KANTREX should be used by intravenous infusion only when the intramuscular route is impracticable. KANTREX can also be employed for intraperitoneal use, aerosol treatment, and as an irrigating solution. See package insert for directions.

PRECAUTIONS

Use of antibiotics may occasionally result in overgrowth of non-sensitive organisms. If superinfection appears during therapy, appropriate measures should be taken.

SUPPLY

Available in rubber-capped vials as a ready-to-use sterile aqueous solution in two concentrations (stable at room temperature indefinitely):

KANTREX Injection, 0.5 Gm. kanamycin (as sulfate) in 2 ml. volume.
KANTREX Injection, 1.0 Gm. kanamycin (as sulfate) in 3 ml. volume.

CAPSULES (for local gastrointestinal therapy; not for systemic medication)

INDICATIONS AND DOSAGE

For preoperative bowel sterilization: 1.0 Gm. (2 capsules) every hour for 4 hours, followed by 1.0 Gm. (2 capsules) every 6 hours for 36 to 72 hours.

For intestinal infections: Adults: 3.0 to 4.0 Gm. (6 to 8 capsules) per day in divided doses for 5 to 7 days. Infants and children: 50 mg. per kg. per day in 4 to 6 divided doses for 5 to 7 days.

PRECAUTION

Preoperative use of KANTREX Capsules is contraindicated in the presence of intestinal obstruction. Although only negligible amounts of KANTREX are absorbed through intact intestinal mucosa, the possibility of increased absorption from ulcerated or denuded areas should be considered.

SUPPLY

KANTREX Capsules, 0.5 Gm. kanamycin (as sulfate), bottles of 20 and 100.

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For the first time

CONVENIENCE and ECONOMY

for that all-important first dose of broad-spectrum antibiotic therapy

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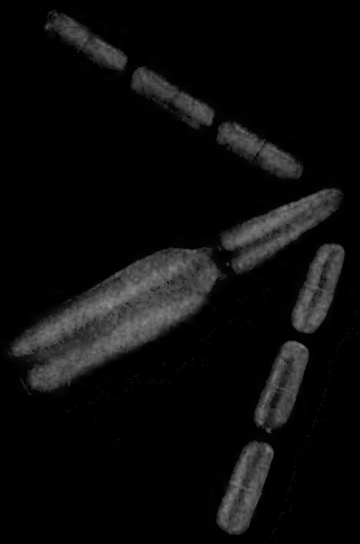
TERRAMYCIN®
brand of oxytetracycline

INTRAMUSCULAR SOLUTION



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...and for continued, compatible, coordinated therapy

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oxytetracycline with glucosamine

CAPSULES

Continuation with oral Cosa-Terramycin every six hours will provide highly effective antibacterial serum and tissue levels for prompt infection control.

The unsurpassed record of clinical effectiveness and safety established for Terramycin is your guide to successful antibiotic therapy.

Supply:
*Terramycin Intramuscular Solution**
100 mg./2 cc. ampules
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Cosa-Terramycin Capsules
125 mg. and 250 mg.

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Lifts depression...

An emotionally balanced patient
Thanks to your treatment and the help of Deprol, her depression is relieved and her anxiety and tension calmed. She eats well, sleeps well, and can return to her normal activities.

as it calms anxiety!

Deprol helps balance the mood by lifting depression as it calms related anxiety

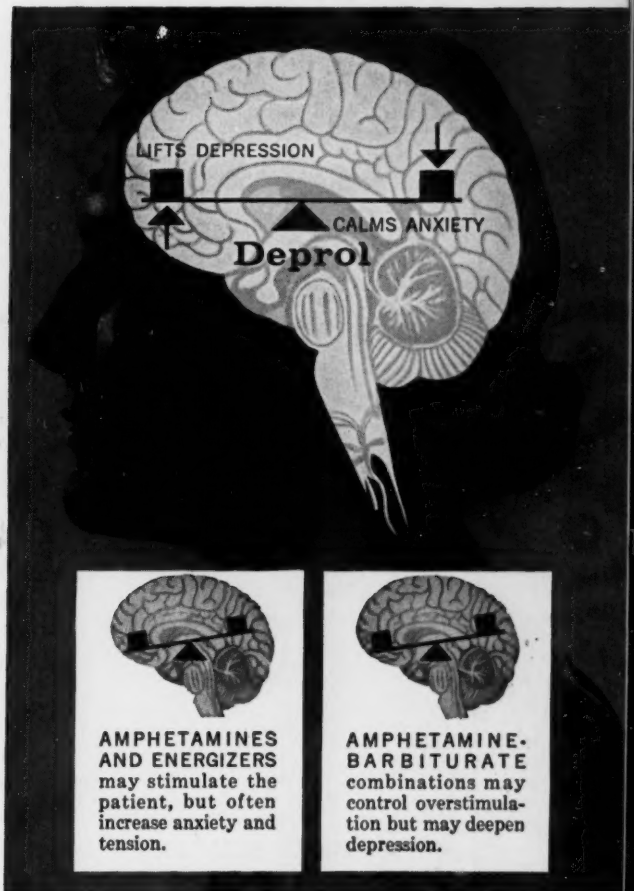
No "seesaw" effect of amphetamine-barbiturates and energizers

While amphetamines and energizers may stimulate the patient—*they often aggravate anxiety and tension.* And although amphetamine-barbiturate combinations may counteract excessive stimulation—*they often deepen depression.*

In contrast to such "seesaw" effects, Deprol lifts depression as it calms anxiety—both at the same time.

Safer choice of medication than untested drugs

Deprol does not produce hypotension, liver damage, psychotic reactions or changes in sexual function.


LIFTS DEPRESSION
CALMS ANXIETY
Deprol
AMPHETAMINES AND ENERGIZERS may stimulate the patient, but often increase anxiety and tension.
AMPHETAMINE-BARBITURATE combinations may control overstimulation but may deepen depression.

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▲Deprol▲®

DOSAGE: Usual starting dose is 1 tablet q.i.d. When necessary, this may be gradually increased up to 3 tablets q.i.d.

COMPOSITION: 1 mg. 2-diethylaminoethyl benzilate hydrochloride (benactyzine HCl) and 400 mg. meprobamate.

SUPPLIED: Bottles of 50 light-pink, scored tablets. Write for literature and samples.

WALLACE LABORATORIES / *New Brunswick, N. J.*

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NOW... SAFER, EFFECTIVE TRANQUILIZER THERAPY

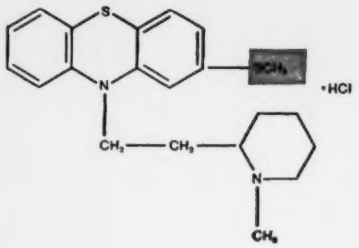
greater specificity
of tranquilizing action
—divorced from such
"diffuse" effects as
anti-emetic action
—explains why

THIORIDAZINE HCl

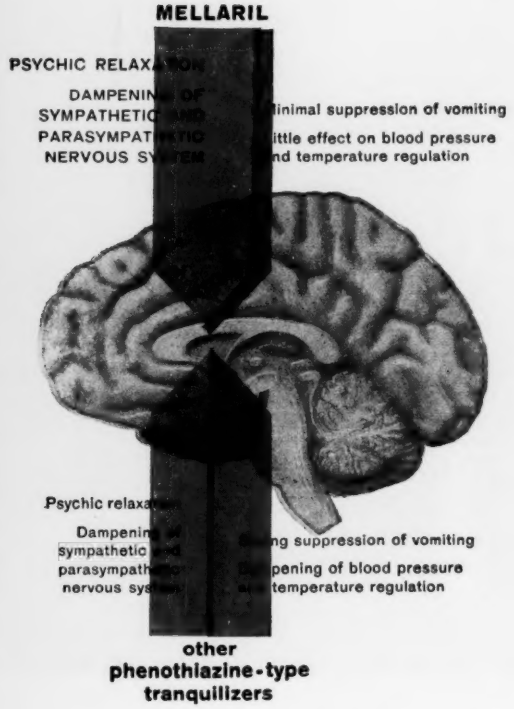
is virtually free of such toxic effects as jaundice, Parkinsonism, blood dyscrasia

"Thioridazine [MELLARIL] is a piperidine derivative of the basic phenothiazine but with appreciably less toxic effects than those usually attributed with other phenothiazines. This drug appears to represent a major addition to the [illegible] effective treatment of a wide range of psychological disturbances seen daily in the clinics or by the general practitioner."

a new advance in tranquilization:
greater specificity of tranquilizing action results in fewer side effects



The presence of a thiomethyl radical (S-CH_3) is unique in Mellaril and could be responsible for the relative absence of side effects and greater specificity of psychotherapeutic action. This is shown clinically by:


MELLARIL
PSYCHIC RELAXATION
DAMPENING OF SYMPATHETIC AND PARASYMPATHETIC NERVOUS SYSTEM
Minimal suppression of vomiting
Little effect on blood pressure and temperature regulation
Psychic relaxation
Dampening of sympathetic and parasympathetic nervous system
Suppression of vomiting
Dampening of blood pressure and temperature regulation
other phenothiazine-type tranquilizers

1 A specificity of action on certain brain sites in contrast to the more generalized or "diffuse" action of other phenothiazines. This is evidenced by a lack of appreciable anti-emetic effect.

2 Less "spill-over" action to other brain areas — hence, absence of undue sedation, drowsiness or autonomic nervous system disturbances.

3 A notable absence of extrapyramidal stimulation.

4 Lack of impairment of patient's normal drive and energy.

5 Virtual freedom from such toxic effects as jaundice, photosensitivity, skin eruptions, blood forming disorders.

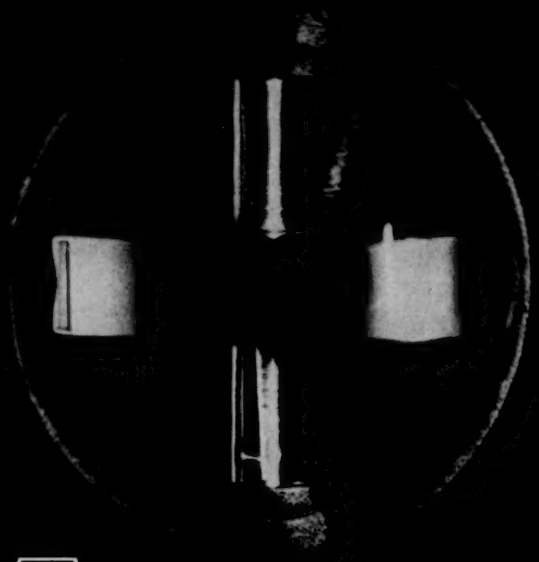
INDICATION	USUAL STARTING DOSE	TOTAL DAILY DOSAGE RANGE
ADULTS: Mental and Emotional Disturbances:		
MILD—where anxiety, apprehension and tension are present	10 mg. t.i.d.	20-60 mg.
MODERATE—where agitation exists in psychoneuroses, alcoholism, intractable pain, senility, etc.	25 mg. t.i.d.	50-200 mg.
SEVERE—in agitated psychotic states as schizophrenia, manic depressive, toxic psychoses, etc.:		
Ambulatory	100 mg. t.i.d.	200-400 mg.
Hospitalized	100 mg. t.i.d.	200-800 mg.
CHILDREN: BEHAVIOR PROBLEMS IN CHILDREN	10 mg. t.i.d.	20-40 mg.

MELLARIL Tablets, 10 mg., 25 mg., 100 mg.

*Ostfeld, A. M.: Scientific Exhibit, American Academy of General Practice, San Francisco, April 6-9, 1959

SANDOZ

minimal disturbance
of the patient's chemical and psychic balance . . .



still unsurpassed for total corticosteroid benefits

Aris

Substantiated by published reports of leading clinicians:

- **effective control** of allergic and inflammatory symptoms[1-20]
- **minimal disturbance** of the patient's chemical and psychic balance[1, 4, 5, 8-19]

tocort®

Triamcinolone LEDERLE

At anti-inflammatory and antiallergic levels ARISTOCORT means:

- **freedom from salt and water retention**
- **virtual freedom from potassium depletion**
- **negligible calcium depletion**
- **euphoria and depression rare**
- **no voracious appetite—no excessive weight gain**
- **low incidence of peptic ulcer**
- **low incidence of osteoporosis with compression fracture**

Indications: rheumatoid arthritis; arthritis; respiratory allergies; allergic and inflammatory dermatoses; disseminated lupus erythematosus; nephrotic syndrome; lymphomas and leukemias. *Precautions:* With ARISTOCORT all traditional precautions to corticosteroid therapy should be observed. Dosage should always be carefully adjusted to the smallest amount which will suppress symptoms. After patients have been on steroids for prolonged periods, discontinuance must be carried out gradually.
Supplied: Scored tablets of 1 mg. (yellow); 2 mg. (pink); 4 mg. (white); 16 mg. (white). Diacetate Parenteral (for intra-articular and intrasynovial injection). Vials of 5 cc. (25 mg./cc.).

References: 1. Feinberg, S.M., Feinberg, A.R., and Fisherman, E.W.: *J.A.M.A.* 167:58 (May 3) 1958. 2. Epstein, J.I. and Sherwood, H.: *Connecticut Med.* 22:822 (Dec.) 1958. 3. Friedlaender, S. and Friedlaender, A.S.: *Antibiotic Med. & Clin. Ther.* 5:315 (May) 1958. 4. Segal, M.S. and Duvenci, J.: *Bull. Tufts North East M. Center* 4:71 (April-June) 1958. 5. Segal, M.S.: Report to the A.M.A. Council on Drugs, *J.A.M.A.* 169:1063 (March 7) 1958. 6. Sherwood, H. and Cooke, R.A.: *J. Allergy* 28:97 (Mar.) 1958. 7. Duke, C.J. and Oviedo, R.: *Antibiotic Med. & Clin. Ther.* 5:710 (Dec.) 1958. 8. McGavack, T.H.: *Clin. Med.* (June) 1958. 9. Freyberg, R.H.; Berntsen, C.A., and Hellman, L.: *Arthritis and Rheumatism* 1:215 (June) 1958. 10. Hartung, E.F.: *J.A.M.A.* 167:973 (June 21) 1958. 11. Hartung, E.F.: *J. Florida Acad. Gen. Pract.* 8:18, 1958. 12. Zuckner, J.; Ramsey, R.H.; Caciolo, C., and Gantner, G.E.: *Ann. Rheum. Dis.* 17:398 (Dec.) 1958. 13. Appel, B.; Tye, M.J., and Leibsohn, E.: *Antibiotic Med. & Clin. Ther.* 5:716 (Dec.) 1958. 14. Kalz, F.: *Canad. M.A.J.* 79:400 (Sept.) 1958. 15. Mullins, J.F., and Wilson, C.J.: *Texas State J. Med.* 54:648 (Sept.) 1958. 16. Shelley, W.B.; Harun, J.S., and Pillsbury, D.M.: *J.A.M.A.* 167:959 (June 21) 1958. 17. DuBois, E.F.: *J.A.M.A.* 167:1590 (July 26) 1958. 18. McGavack, T.H.; Kao, K.T.; Leake, D.A.; Bauer, H.G., and Berger, H.E.: *Am. J. Med. Sc.* 236:720 (Dec.) 1958. 19. Council on Drugs: *J.A.M.A.* 169:257 (Jan. 17) 1959. 20. Rein, C.R.; Fleischmajer, R., and Rosenthal, A.R.: *J.A.M.A.* 165:1821 (Dec. 7) 1957.

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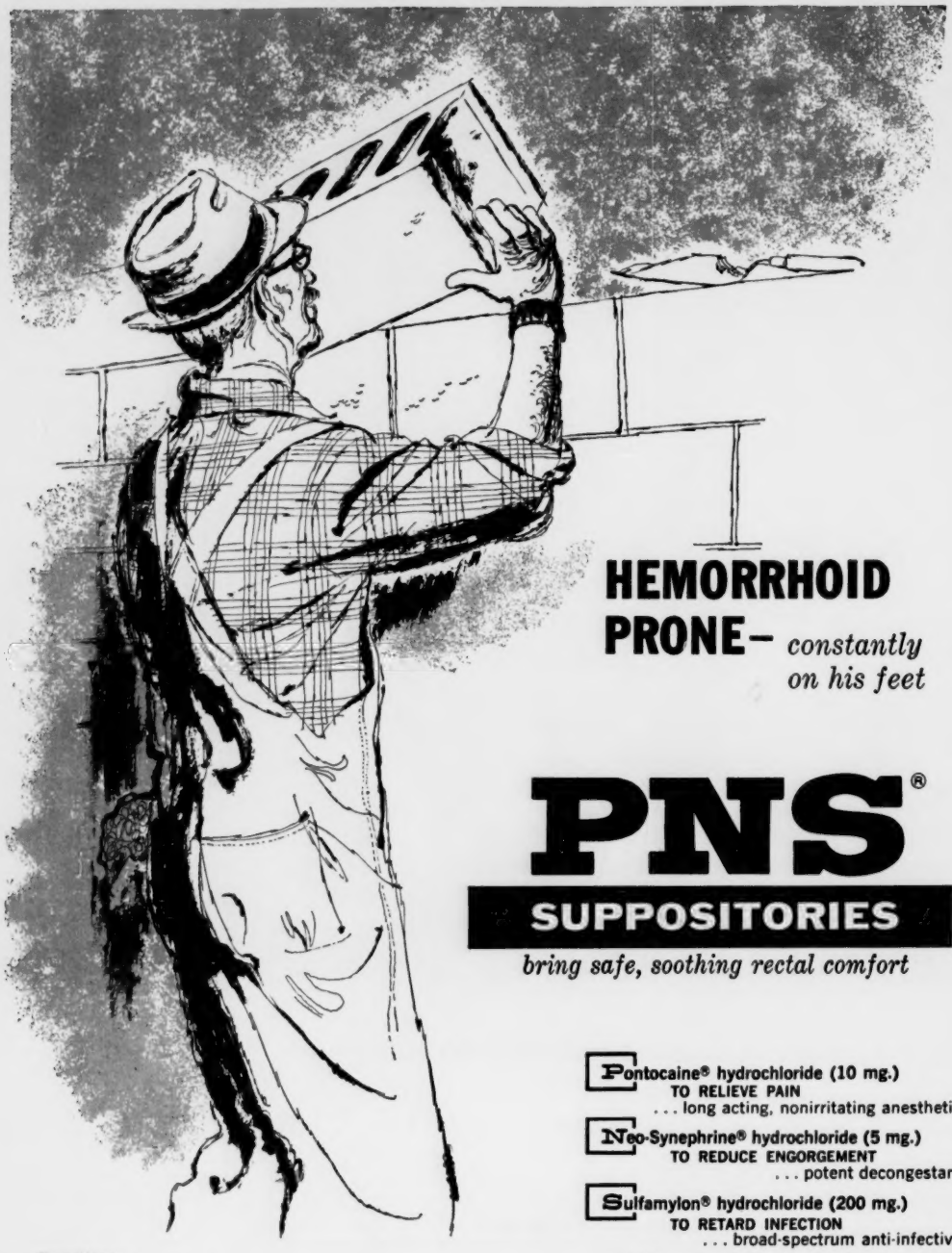

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The first synthetic penicillin available for general clinical use

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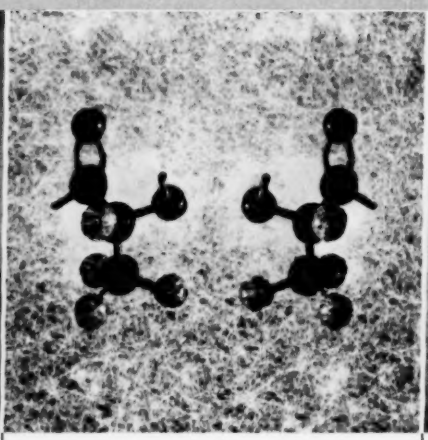
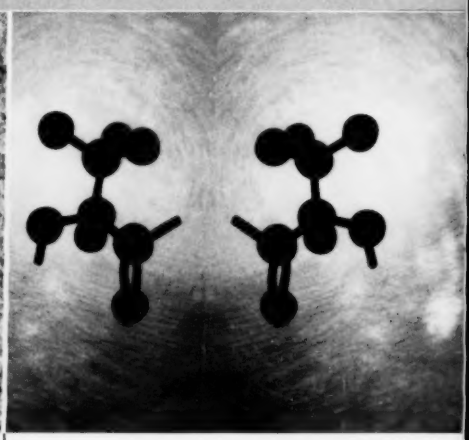
SYNC





BLOOD LEVELS TWICE AS HIGH AS WITH POTASSIUM PENICILLIN V

SAFER ORAL ROUTE PROVIDES HIGHER BLOOD LEVELS THAN INTRAMUSCULAR PENICILLIN G

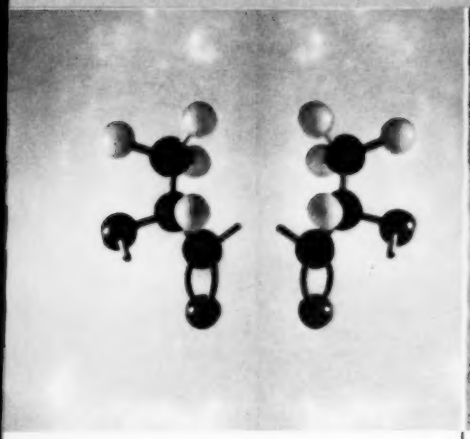
IMPROVED ANTIBIOTIC EFFECT FROM COMPLEMENTARY ACTION OF ISOMERS

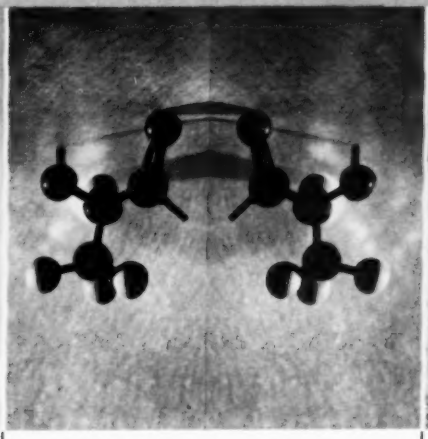
ORIGIN OF A NEW

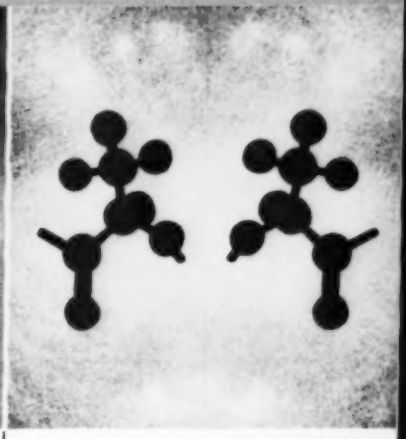
ADVANTAGES ACCOMPANY MOLECULAR ASYMMETRY

ILLIXIN™

POTASSIUM PENICILLIN-152







ANTIBIOTIC ACTIVITY DIRECTLY PROPORTIONAL TO ORAL DOSE

REDUCED HAZARD OF SERIOUS ALLERGENICITY BY SAFER ORAL ROUTE

MANY STAPH STRAINS MORE SENSITIVE TO SYNCILLIN

BRISTOL

ISOMERIC COMPLEMENTARITY

ORIGIN OF A NEW SYNTHETIC PENICILLIN

In March, 1957, Dr. John C. Sheehan of the Massachusetts Institute of Technology announced the total synthesis of penicillin from common raw materials, thus solving a problem which had baffled research workers for more than 15 years. Although total synthesis was not commercially practicable, this work, sponsored by Bristol Laboratories, made possible the subsequent synthesis of new penicillins not occurring in nature. Later scientists at Beecham Laboratories in England discovered that a key intermediate (6-aminopenicillanic acid) could be produced by a fermentation process. With these achievements, large scale production of synthetic penicillins became feasible.

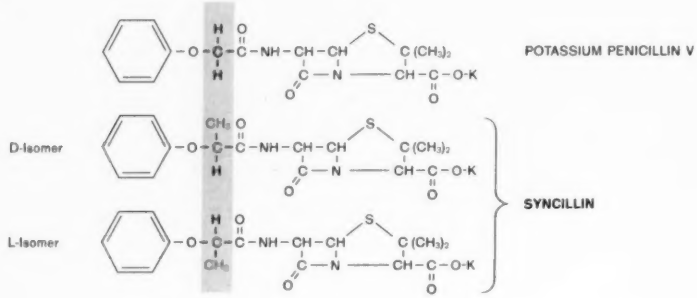
Organic chemists at Bristol then embarked upon an intensive program to develop better penicillins. Over five hundred were synthesized and underwent preliminary screening. Forty-six showed sufficient promise to warrant further investigation. Extensive microbiological, pharmacological, and clinical screening indicated that one compound, SYNCILLIN, had advantages of major importance over other penicillins.

SYNCILLIN is the N-acylation product of 6-aminopenicillanic acid and α-phenoxypropionic acid (the phenylether of lactic acid). It is freely soluble in water and remarkably resistant to decomposition by acid. The acid stability of SYNCILLIN is equivalent to that of penicillin V at pH 2 and pH 3 at 37° C.[1]

SIGNIFICANCE OF MOLECULAR ASYMMETRY AND ISOMERIC COMPLEMENTARITY

SYNCILLIN has a molecular configuration similar to penicillin V, but contains an additional CH_3 group so positioned as to render the adjacent carbon atom asymmetric. (In the formulae below, the added CH_3 group is shown in blue and the asymmetric carbon atom in red.) As a result, SYNCILLIN occurs as a mixture of two isomers.

Each isomer has been synthesized in essentially pure form and found to possess distinctive chemical and biological properties. The L-isomer is 2 to 17 times more active than the D-isomer against many of the organisms tested. As produced, SYNCILLIN is a mixture of the L-isomer and the D-isomer. As will be shown later, the antibiotic effect of the clinically available mixture, SYNCILLIN, is greater than either isomer alone against many organisms. This phenomenon is referred to here as *isomeric complementarity*.



SYNCILLIN

major therapeutic advantages accompany molecular asymmetry

ISOMERIC COMPLEMENTARITY

ISOMERIC COMPLEMENTARITY DEMONSTRATED IN VITRO

The *in vitro* minimum inhibitory concentration (MIC) of SYNCILLIN and of each of its two component isomers was determined for a variety of common pathogens and laboratory test organisms. As may be seen from Table 1, all three are highly effective against penicillin-susceptible staphylococci and against pneumococci, streptococci, gonococci, and corynebacteria; all are ineffective against Salmonella, *E. coli,* and other gram-negative coliform bacilli.

SYNCILLIN was more active against many of the test strains including some streptococci and staphylococci than either of its components. This demonstrates *in vitro* the phenomenon of isomeric complementarity.

TABLE 1

Minimum Concentrations of SYNCILLIN and Components Required to Inhibit a Wide Range of Bacteria

SYNCILLIN

major therapeutic advantages accompany molecular asymmetry

Of equal interest are the findings of White.[3] Six penicillin-resistant strains of staphylococci were isolated from hospital infections. None was sensitive to potassium penicillin V. All

ISOMERIC COMPLEMENTARITY CONFIRMED IN VIVO

To determine the median curative dose (CD_{50}) mice were infected with 100 times the lethal dose of *Staphylococcus aureus*. Each penicillin being tested was administered intramuscularly at the same time, and the dose required to cure half the animals determined. The greater effect of the mixture of the two isomers (SYNCILLIN) is shown in two independent experiments. (See Figure 1.) Note that isomeric complementarity is thus confirmed *in vivo*.

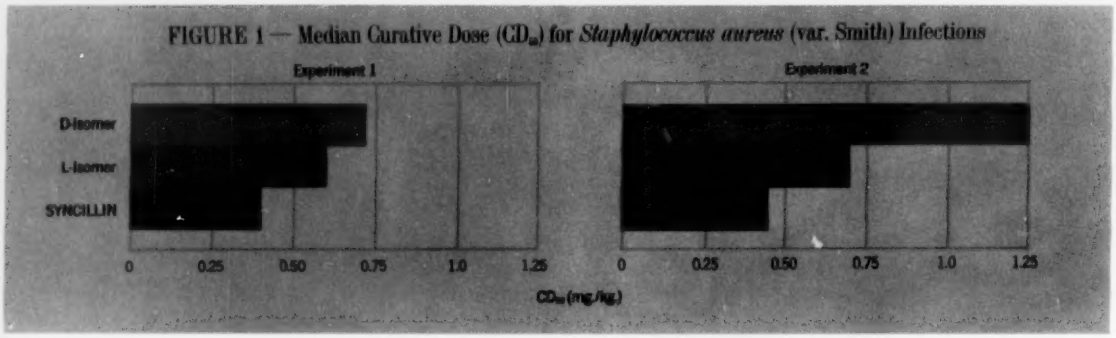


FIGURE 1 — Median Curative Dose (CD_{50}) for *Staphylococcus aureus* (var. Smith) Infections

MANY STRAINS OF STAPHYLOCOCCI MORE SENSITIVE TO SYNCILLIN

SYNCILLIN has been tested against a large number of strains of *Staphylococcus aureus* isolated from clinical sources. Many organisms resistant to potassium penicillin G and potassium penicillin V proved sensitive to SYNCILLIN.

Wright[2] performed sensitivity studies on 54 strains, the majority of which were resistant or moderately resistant to penicillin V and penicillin G. Thirty-two (60%) of the strains were sensitive to SYNCILLIN, approximately twice as many as with the other penicillins. (See Figure 2.) In two-thirds of the isolates, SYNCILLIN produced inhibition at concentrations lower than those required for either of the other antibiotics. One strain was more sensitive to penicillin G.

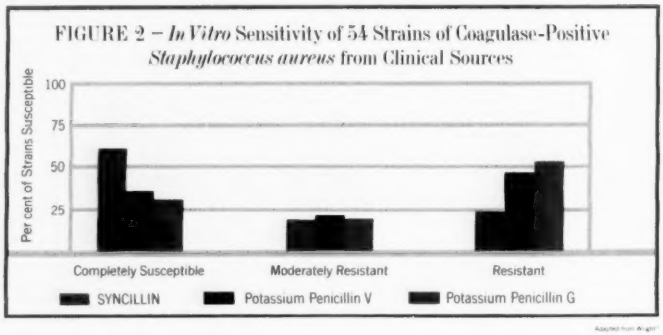


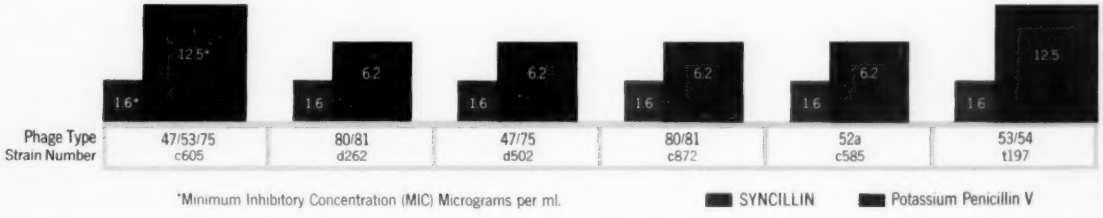
FIGURE 2 — *In Vitro* Sensitivity of 54 Strains of Coagulase-Positive *Staphylococcus aureus* from Clinical Sources

ISOMERIC COMPLEMENTARITY

Of equal interest are the findings of White.[3] Six penicillin-resistant strains of staphylococci were isolated from hospital infections. None was sensitive to potassium penicillin V. All were sensitive to SYNCILLIN. (See Figure 3.)

FIGURE 3

Minimum Concentrations of SYNCILLIN Required to Inhibit
Hospital Strains of *Staphylococcus aureus* Resistant to Potassium Penicillin V

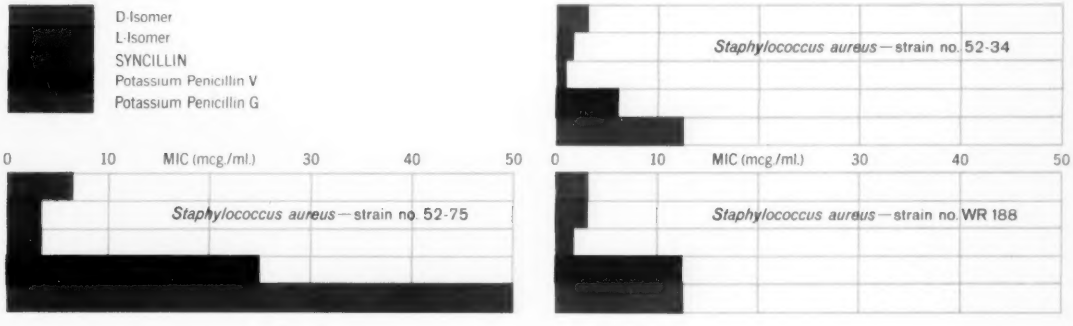


The efficacy of SYNCILLIN against the type 80/81 Staphylococcus (dangerous and widespread in hospitals) is worthy of special attention.

The complementary action of the component isomers is also seen with strains of staphylococci resistant to penicillins. Note that SYNCILLIN is more effective than either isomer against strains 52-34 and WR 188. (See Figure 4.) Against all three strains, SYNCILLIN is effective at concentrations below serum levels, while penicillins V and G are ineffective.

FIGURE 4

Minimum Inhibitory Concentrations (MIC) for Coagulase-Positive
Penicillin-Resistant Strains of *Staphylococcus aureus*



Isomeric complementarity has thus been demonstrated for:

— *certain penicillin-susceptible streptococci, staphylococci and corynebacteria* in vitro *(Table 1)*

— *penicillin-susceptible staphylococci* in vivo *(Figure 1)*

— *penicillin-resistant staphylococci* in vitro *(Figure 4)*

SYNCILLIN

major therapeutic advantages accompany molecular asymmetry

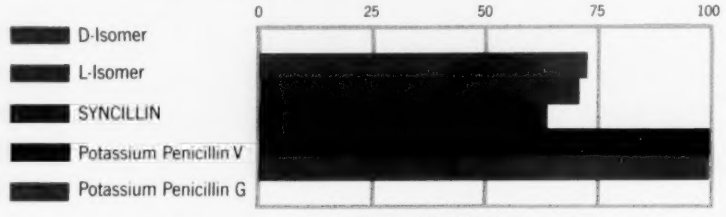
BLOOD LEVELS TWICE AS HIGH AS WITH

ISOMERIC COMPLEMENTARITY SHOWN BY REDUCED RATE OF INACTIVATION BY PENICILLINASE

Bacterial resistance to penicillin has been attributed to the action of penicillin-inactivating enzymes produced by the invading organisms.[4] As shown in Figure 5, SYNCILLIN is less affected by staphylococcal penicillinase than either of its component isomers – a further demonstration of isomeric complementarity. Further, SYNCILLIN is shown to be less inactivated by this enzyme than penicillin V and penicillin G.

Resistance to SYNCILLIN develops in a slow, step-wise manner characteristic of other penicillins, in contrast to the usually rapid development of resistance to streptomycin.

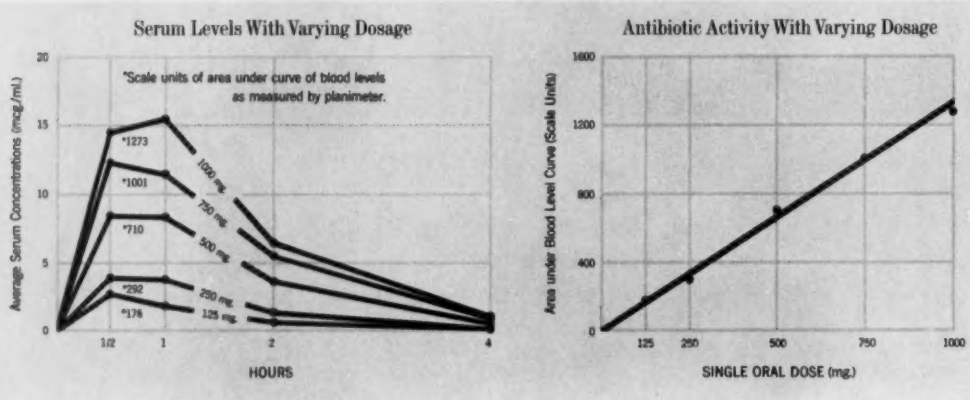
FIGURE 5—Effect of Staphylococcal Penicillinase on Different Penicillins



ANTIBIOTIC ACTIVITY DIRECTLY PROPORTIONAL TO ORAL DOSAGE

Cronk[5] studied blood levels after administering varying amounts of SYNCILLIN. (Figure 6.) Total antibiotic activity (obtained by measuring areas under curves with a planimeter) increases rapidly as the dose is doubled. These data show that increased dosage markedly increases serum concentration and thus may enhance the drug's effectiveness.

FIGURE 6



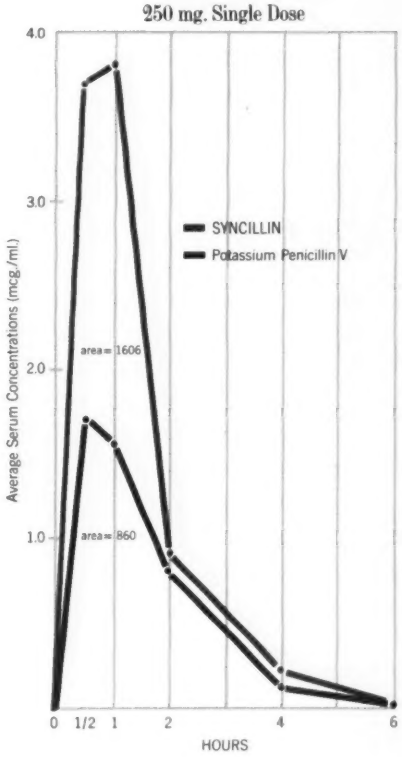
BLOOD LEVELS TWICE AS HIGH AS WITH POTASSIUM PENICILLIN V AFTER ORAL ADMINISTRATION

Wright[6] performed comparative crossover blood level studies on volunteer subjects receiving equivalent amounts of potassium penicillin V and SYNCILLIN. The peak concentrations attained during the first hour after administration were twice as high with SYNCILLIN.

The total antibiotic activity as measured by the area under the curves (see Figure 7) indicates an almost 2 to 1 superiority of SYNCILLIN (1606) over potassium penicillin V (860).

The higher blood levels may be of value with organisms of only moderate penicillin-sensitivity where doubling the blood concentration may be essential for effective bactericidal action. In addition these higher levels may be necessary where there is infection in areas with a poor blood supply.[7] Under these circumstances a higher blood concentration may provide the increased diffusion pressure required to deliver adequate amounts to the tissue.

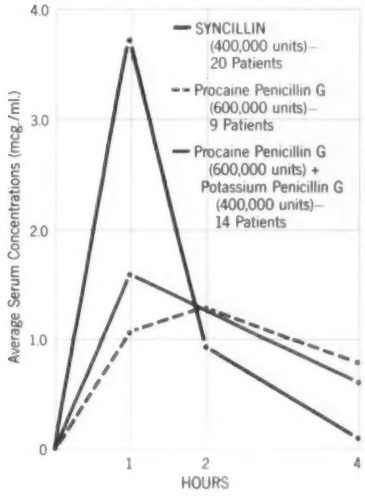
FIGURE 7
20 Subject Crossover
250 mg. Single Dose



BLOOD LEVELS MUCH HIGHER THAN WITH INTRAMUSCULAR PENICILLIN G

In addition, blood levels attained with oral SYNCILLIN[6] are much higher than those with intramuscular penicillin G.[8a, b] (See Figure 8.) Note that the level at one hour for SYNCILLIN (3.8 mcg./ml.) is more than twice as high as with procaine penicillin G, even when reinforced with potassium penicillin G (1.6 mcg./ml.). Since penicillins are *bactericidal,* these intermittent high serum levels can be clinically significant. Thus, SYNCILLIN offers the promise of superior efficacy via the safer oral route.

FIGURE 8—Serum Levels after Oral Administration of SYNCILLIN (250 mg.) and after Intramuscular Injection of Penicillin G



SYNCILLIN

major therapeutic advantages accompany molecular asymmetry

REDUCED HAZARD OF SERIOUS ALLERGENICITY BY SAFER ORAL ROUTE

SYNCILLIN has been administered in multiple doses to 437 patients and volunteers. One patient developed itching during therapy, possibly an allergic side effect. Another had a purpuric rash, but no relationship to SYNCILLIN was established. No reactions were observed in 9 patients with a known history of sensitivity to penicillin.

While the above data suggests the possibility of reduced allergenic hazard, no definite conclusions may be drawn at this time. *The usual precautions for oral penicillin therapy should be observed.* Patients with histories of asthma, hay fever, urticaria, or previous penicillin-sensitivity should especially be watched carefully. Since SYNCILLIN is administered orally, it may be expected to be safer than parenteral penicillin.

As Flippin[9] recently stated, "... it is well established that serious allergy to the drug [penicillin] is most likely to occur following parenteral administration, especially after repeated intramuscular injections; the oral route is least likely to initiate severe hypersensitivity reactions. This can be explained partly by the fact that when reactions develop following oral medication, they are usually slow enough to treat symptomatically; thus the progression of the reaction can usually be interrupted. . . . In view of the relatively high incidence of severe allergy to injectable penicillin, it would seem advisable to employ oral penicillin routinely, except in the control of infections involving the blood stream, endocardium, meninges, etc., in which cases the parenteral route remains the preferred treatment."

SYNCILLIN, like other penicillins, is essentially free of other toxicity. No hematopoietic, hepatic, or renal toxicity was observed in 210 volunteers receiving 1 gm. daily for 2 to 3 weeks.[10]

CLINICAL EFFICACY DEMONSTRATED IN PENICILLIN-SENSITIVE INFECTIONS

Clinical trials conducted by Blau and Kanof,[11] White,[12] Prigot,[13] Robinson,[14] Dube,[15] Ferguson,[16] Rutenburg,[17] Richardson,[18] Bunn,[19] Cronk,[5] Kligman,[10] and Yow [20] demonstrated the efficacy of SYNCILLIN in a variety of streptococcal, staphylococcal, pneumococcal, and gonococcal infections. Conditions treated included respiratory, skin, soft tissue, wound, and chronic urinary tract infections; acute gonorrhea; cellulitis; septicemia; otitis media; gingivitis; and Vincent's angina. In a few patients SYNCILLIN was used for rheumatic fever or gonorrheal prophylaxis.

One hundred seventy-two of one hundred ninety-six patients responded favorably to SYNCILLIN. The failures included 1 patient with pustular dermatoses, 10 elderly patients with chronic urinary tract infections, 1 patient with gonorrhea, 1 patient with a gram-negative infection, and 10 patients with staphylococcal infections. Lack of response of staphylococcal infections was attributed to the presence of resistant organisms or local suppurative foci requiring drainage.

SYNCILLIN

major therapeutic advantages accompany molecular asymmetry

Relatively few side effects were encountered. One patient experienced moderate itching of the skin which was controlled by an antihistamine. Another reported pruritus ani which did not interfere with therapy. Diarrhea occurred in 4 instances. There was one purpuric rash, but no relationship to SYNCILLIN could be established.

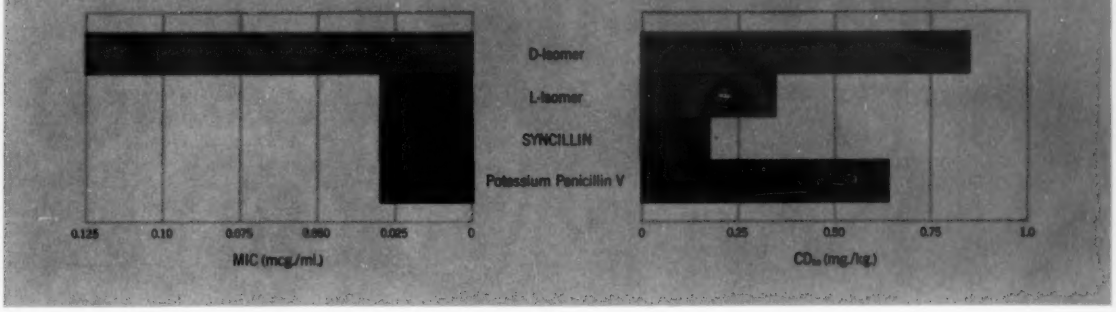
Clinical response usually begins within 24 hours in infections susceptible to SYNCILLIN. Recovery occurs in 4 to 7 days depending upon the severity of the infection. Gonorrheal infections respond very promptly to SYNCILLIN; 500 mg. b.i.d. for two days usually produce bacteriologic cures.

IMPROVED ANTIBIOTIC EFFECT FROM COMPLEMENTARY ACTION OF ISOMERS

SYNCILLIN is a mixture of isomers. The L-isomer is 2 to 17 times more active than the D-isomer against many of the organisms tested. Furthermore, the D- and L-isomers have other distinguishing chemical, pharmacological, and microbiological properties. Their *in vivo* and *in vitro* activities differ for many important pathogens. *Against many of the organisms tested, the combination of isomers* (SYNCILLIN) *is much more active than the stronger isomer alone.* This phenomenon of isomeric complementarity is not always demonstrable, for in a few instances SYNCILLIN is slightly less active.

Isomeric complementarity has previously been demonstrated *in vitro* (Figure 4) and *in vivo* (Figure 1). Figure 9 reveals a third form of superiority related to isomeric complementarity. Equal concentrations of SYNCILLIN and penicillin V were required to inhibit this growth of staphylococci *in vitro.* But, *in vivo,* a much smaller amount of SYNCILLIN *(one-third that of penicillin V)* was effective in an experimental infection with the same strain. These observations on complementary action indicated the advantage of producing the mixture of isomers as the medication to be made available for clinical therapy.

FIGURE 9 — Comparison of CD_m and MIC Values Against *Staphylococcus aureus* (var. Smith)



Isomeric complementarity has thus been demonstrated for:

— *certain penicillin-susceptible streptococci, staphylococci and corynebacteria* in vitro *(Table 1)*

— *penicillin-susceptible staphylococci* in vivo *(Figures 1 and 9)*

— *penicillin-resistant staphylococci* in vitro *(Figure 4)*

— *staphylococcal penicillinase antibiotic inactivation (Figure 5)*

SYNCILLIN

major therapeutic advantages accompany molecular asymmetry

Indications:

SYNCILLIN is recommended in the treatment of infections caused by pneumococci, streptococci, gonococci, corynebacteria, and penicillin-sensitive staphylococci. In addition, SYNCILLIN is effective against certain strains of staphylococci resistant to other penicillins.

SYNCILLIN, like other oral penicillins, is not recommended at the present time in deep-seated or chronic infections, subacute bacterial endocarditis, meningitis, or syphilis.

Dosage:

125 mg. or 250 mg. three times daily, depending on the severity of infection. Larger doses (e.g., 500 mg. t.i.d.) may be used for more severe infections. SYNCILLIN may be administered without regard to meals.

Beta hemolytic streptococcal infections should be treated with SYNCILLIN for at least ten days.

Precautions:

While present data suggest the possibility of reduced allergenic hazard, no definite conclusions may be drawn at this time. *Therefore the usual precautions with oral penicillin therapy must be observed.* Patients with histories of asthma, hay fever, urticaria, or previous reactions to penicillin should be watched with special care.

Diarrhea has been reported occasionally following heavy dosage. If this occurs, the interval between dosages should be lengthened.

If superinfection occurs during therapy, appropriate measures should be taken.

Since some strains of staphylococci are resistant to SYNCILLIN as well as to other penicillins, cultures and sensitivity tests should be performed where indicated by clinical judgment. As is true with all antibiotics, clinical response does not always correlate with laboratory bacterial sensitivity reports.

Supply:

125 and 250 mg. tablets, bottles of 25 and 100. 125 mg. powder for oral solution, 60 ml. vials.

References: 1. Lein, J.: Microbiology report to Bristol Laboratories Inc. 2. Wright, W. W.: Microbiology report to Bristol Laboratories Inc. 3. White, A. C.: Microbiology report to Bristol Laboratories Inc. 4. Dubos, R. J.: Bacterial and Mycotic Infections of Man, 3rd edition, Philadelphia, J. B. Lippincott Co., p. 690. 5. Cronk, G. A.: Clinical report to Bristol Laboratories Inc. 6. Wright, W. W.: Clinical report to Bristol Laboratories Inc. 7. Kass, E. H.: Am. J. Med. *18*:764 (May) 1955. 8a. White, A. C.; Couch, R. A.; Foster, F.; Calloway, J.; Hunter, W., and Knight, V.: in Welch, H. and Marti-Ibañez, F.: Antibiotics Annual — 1955-1956, Medical Encyclopedia, Inc., New York, 1956, p. 490. b. Data on file — at Bristol Laboratories. 9. Flippin, H. F.: Pennsylvania M. J. *62*:864 (June) 1959. 10. Kligman, A.: Clinical report to Bristol Laboratories Inc. 11. Blau, S., and Kanof, N.: Clinical report to Bristol Laboratories Inc. 12. White, A. C.: Clinical report to Bristol Laboratories Inc. 13. Prigot, A.: Clinical report to Bristol Laboratories Inc. 14. Robinson, C.: Clinical report to Bristol Laboratories Inc. 15. Dube, A. H.: Clinical report to Bristol Laboratories Inc. 16. Ferguson, B.: Clinical report to Bristol Laboratories Inc. 17. Rutenburg, A. M.: Clinical report to Bristol Laboratories Inc. 18. Richardson, J. H.: Clinical report to Bristol Laboratories Inc. 19. Bunn, P. A.: Clinical report to Bristol Laboratories Inc. 20. Yow, E. M.: Clinical report to Bristol Laboratories Inc.

BRISTOL

major therapeutic advantages accompany molecular asymmetry

SYNCILLIN

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1. Kuge, T.: To be published.

H-227

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1. Based on estimate by Van Volkenburgh, V. A., and Frost, W. H.: Am. J. Hygiene 71:122 (Jan.) 1933

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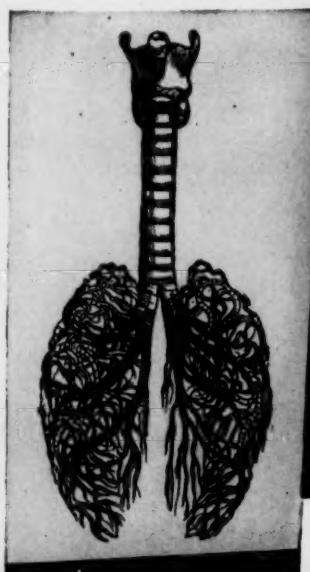

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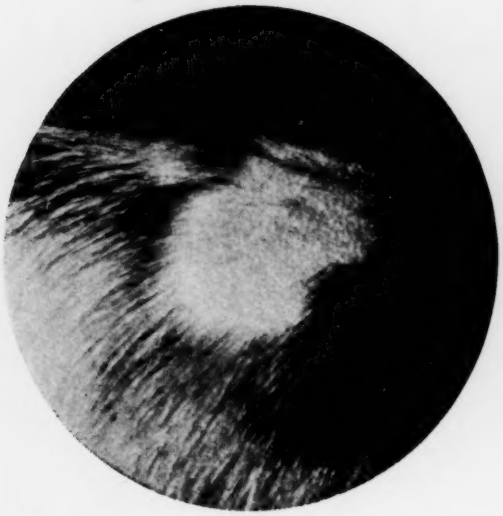

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1. Robinson, H. M., Jr., *et al.*: Griseofulvin, Clinical and Experimental Studies, A.M.A. Arch. Dermat., in press.

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The Practice of Tubal Ligation In North Carolina

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and

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The practice of tubal ligation is a controversial precedure among obstetricians and gynecologists; recently it has become a controversial procedure among the legislators and the citizens of North Carolina. This controversy can be equitably settled only by thoughtful physicians and citizens obtaining basic facts and exercising reasonable judgment. In order to determine the practice of tubal ligation in this state, the hospitals in North Carolina were surveyed by representatives of the University of North Carolina, the State Board of Health, and the chairman of the Sterilization Committee of the North Carolina Obstetrical and Gynecological Society.

Method of Conducting Survey

Letters were sent to 144 of the state's largest hospitals and clinics excluding military installations. The hospitals were asked to furnish information concerning the number of deliveries and tubal ligations on white and Negro patients and their general practices concerning puerperal ligations for the years 1955, 1956, and 1957.

Replies were received from 83 hospitals, or 57.6 per cent of those queried and 40.6 per cent of all the hospitals and clinics in North Carolina. The North Carolina State Board of Health was helpful in furnishing total hospital deliveries by race, and the perinatal mortality of each hospital and clinic in North Carolina. Data from three hospitals were deleted; in two hospitals vaginal hysterectomies were generally employed for sterilization in lieu of tubal ligations, and in one hospital the record room could not distinguish between puerperal tubal ligations and salpingectomies performed for gynecologic disease.

The data obtained covered 169,272 deliveries and 5,209 tubal ligations. The distribution of the sample is given in table 1.

A sizable and adequate sample of deliveries and tubal ligations was obtained from all but the smaller hospitals and clinics in the state. Letters were written to only 34 of the smaller hospitals. Replies were obtained from 79.2 per cent of the larger hospitals, and the total sample represented 61.2 per cent of all of the deliveries in the state for the years 1955, 1956, and 1957.

The incidence of tubal ligation according to hospital deliveries is given in table 2. Arbitrarily, hospitals were divided into four groups; those having less than 250 deliveries a year, those having 251 to 500 deliveries a year, those having 501 to 1,000 deliveries a year, and those delivering more than 1,000 infants per year. The highest number of deliveries for either of the three years determined the group in which the hospital was placed.

Ten of the reporting hospitals did not perform tubal ligations, for religious or medical reasons. The data are presented, therefore, according to whether the hospital performed or did not perform the procedure. It is apparent that the incidence of tubal ligations is 1:32 for all

Read before the Section on Gynecology and Obstetrics, Medical Society of the State of North Carolina, Asheville, May 6, 1959.

From the Department of Obstetrics and Gynecology, University of North Carolina, School of Medicine, Chapel Hill, North Carolina.

Table 1

Distribution of Data According to the Size of Hospitals Answering Questionnaire (1955-1957)

No. Annual Hospital Deliveries	No. Hospitals and Clinics in North Carolina	No. Answering Questionnaire	% Answering Questionnaire	Total No. Deliveries in N. C. Hospitals and Clinics	Total No. Deliveries in Hospitals or Clinics Answering Questionnaire	% Deliveries in Hospitals Answering Questionnaire
Less than 250	87	12	13.8	25,557	3,760	14.7
251-500	38	23	60.5	40,952	22,518	55.0
501-1000	48	26	54.2	102,206	55,185	54.3
Over 1000	24	19	79.2	107,911	87,809	81.4
Total	197	80	40.6	276,626	169,272	61.2

Table 2

Incidence of Tubal Ligations According to Hospital Deliveries (1955-1957)

	Deliveries	Ligations	Incidence
Hospitals having less than 250 Deliveries per year	3760	105	1:36
Hospitals having less than 250 deliveries per year and performing tubal ligations	2743	105	1:26
Hospitals having 251 to 500 deliveries per year	22,518	674	1:33
Hospitals having 251 to 500 deliveries per year and performing tubal ligations	19,741	674	1.29
Hospitals having 501 to 1,000 deliveries per year	55,185	2062	1:27
Hospitals having 501 to 1,000 deliveries per year and performing tubal ligations	53,671	2062	1:26
Hospitals having more than 1,000 deliveries per year	87,809	2368	1:37
Hospitals having more than 1,000 deliveries per year and performing tubal ligations	79,621	2368	1:34
Total of all hospitals submitting data	169,272	5209	1:32
Total of all hospitals that performed tubal ligations and submitted data	155,776	5209	1:30

Table 3

Indications for Tubal Ligation According to Hospital Deliveries

		Age	Per Cent	Parity	Per Cent
Hospitals Having Less Than 250 Deliveries Per Year					
Number	9	No. specific Requirement	71	No. specific Requirement	13
Hospitals performing tubal ligations	13%	Minimum age 30 and above	29	3 or more	0
				4 or more	62
				5 or more	25
				6 ormore	0
Hospitals Having 251-500 Deliveries Per Year					
Number of hospitals	19	No specific requirement	73	No specific requirement	21
Hospitals performing tubal ligations	27%	Minimum age 30 and above	27	3 or more	15
				4 or more	29
				5 or more	36

Table 4

Indications for Tubal Ligation

		Age	Per Cent	Parity	Per Cent
Hospitals Having 501 to 1,000 Deliveries Per Year					
Number of hospitals	24	No specific requirement	70	No specific requirement	32
Hospitals performing tubal ligations	34%	Minimum age 30 and above	30	3 or more	24
				4 or more	28
				5 or more	16
Hospitals Having More Than 1,000 Deliveries Per Year					
Number of hospitals	18	No specific requirement	65	No specific requirement	33
Hospitals performing tubal ligations	26%	Minimum age 30 and above	35	3 or more	6
				4 or more	39
				5 or more	22

Table 5A

Indications for Tubal Ligation in Hospitals Performing the Operation In 1 to Every 10 to 20 Deliveries

Classification of Hospitals	Per Cent	Age	Per Cent	Parity	Per Cent
Hospitals with less than 250 deliveries	20	No specific requirement	77	No specific requirement	14
Hospitals with 251-500 deliveries	13	Minimum age 30 and above	33	3 or more	29
Hospitals with 501-1000 deliveries	47			4 or more	43
Hospitals with more than 1,000 deliveries	20			5 or more	14
Total	100		100		100

Table 5B

Indications for Tubal Ligation in Hospitals Performing the Operation In 1 in Every 21-35 Deliveries

Hospitals with less than 250 deliveries	4	No specific requirement	84	No specific requirement	15
Hospitals with 251-1,000 deliveries	39	Minimum age 30 and above	16	3 or more	10
Hospitals with 501-1,000 deliveries	22			4 or more	45
Hospitals with more than 1,000 deliveries	35			5 or more	30
Total	100		100		100

the hospitals reporting and 1:30 for the 70 hospitals performing the operation. The highest incidence of the operation was among the three smaller hospital divisions. There was very little yearly variation in the frequency of tubal ligation in either of the four divisions of hospitals or in the entire sample. In 1955 the incidence was 1:33, in 1956, 1:32, and in 1957, 1:31.

Indications for Tubal Ligations According to the Number of Hospital Deliveries

These data represent the answer to two questions concerning the age and the parity of patients having peurperal ligations:

1. What is the lowest age considered in your hospital for tubal ligations?
2. What is the lowest parity considered in your hospital for tubal ligations?

It is evident that 27 to 35 per cent of the hospitals have adhered to the opinion of Donnelly and Lock[1], who recommended that elective tubal ligation should not be considered in women less than 30 years of age. However, 65 to 73 per cent of the hospitals had no specific minimum age for tubal ligation. There was no specific parity requirement in 13 to 33 per cent of the hospitals. Of greater interest is the finding that 75 per cent of the hospitals having 251 to 500 deliveries a year allow tubal ligation after 4 or more deliveries, and the two larger hospital divisions performed tubal ligations with a parity of 4 and below in 74 and 78 per cent respectively.

Indications for Tubal Ligation According to the Incidence of Ligation

Tables 5 and 6 give the indications for tubal ligation according to four divisions of the incidence of ligation in the state. Table 7 gives the percentage distribution of the incidence of tubal ligation in these four divisions. It is evident that there is very little difference in the indications for tubal ligation in hospitals having various incidence of the procedure. A significant difference is seen only in those hospitals having an incidence of ligation greater than one in 55 deliveries. Forty-four per cent of the hospitals in this group had no minimum age requirement for tubal ligation, but 56 per cent had a minimum age limit of 30. This may be contrasted with the requirement of a minimum age of 30 in 16 to 33 per cent of the other three groups shown in tables 5 and 6. Moreover, a parity of 4 or less is an indication for operation in only 45 per cent of the hospitals in this division, while it is significantly higher in the hospitals of the other three divisions. In 22 per cent of the hospitals having the lowest incidence of tubal ligation, the procedure was performed only for medical indications.

A summary of indications for the 70 hospitals performing tubal ligations is given in table 8. It is aparent that 69 per cent of the hospitals have no minimum age requirement for the operation, and 70 per

Table 6A

Indications for Tubal Ligation in Hospitals Performing the Operation In 1 to Every 36-55 Deliveries

Classification of Hospitals	Per Cent	Age	Per Cent	Parity	Per Cent
Hospitals with less than 250 deliveries	17	No specific requirement	70	Not specified	20
Hospitals with 251-500 deliveries	17	Minimum age 30 and above	30	3 or more	0
Hospitals with 501-1,000 deliveries	58			4 or more	70
Hospitals with more than 1,000 deliveries	8			5 or more	10
Total	100		100		100

Table 6B

Indications for Tubal Ligation in Hospitals Performing the Operation In 1 to Every 55 or More Deliveries

Hospitals with less than 250 deliveries	10	No specific requirement	44	No specific requirement	11
Hospitals with 251-500 deliveries	35	Minimum age 30 and above	56	3 or more	11
Hospitals with 501-1,000 deliveries	25			4 or more	23
Hospitals with more than 1,000 deliveries	30			5 or more	33
				operation performed for medical indication only	22%
Total	100		100		100

Table 7

Percentage Distribution of the Incidence of Tubal Ligation Among Hospitals Performing the Operation

Incidence (Ratio of Ligations to Deliveries)	Percentage of Hospitals
1:10-20	28
1:21-35	25
1:36-55	22
1: over 55	25

cent allow tubal ligation on, for or in patients who have a parity of 4 or less.

In an effort to interpret the practice of tubal ligation in each hospital, two questions were asked: 1. In your hospital, are minor medical problems used as indications for tubal ligation when the operation is actually performed for convenience or socioeconomic indications? 2. In your hospital, are tubal ligations performed only for major medical indications? Table 9 summarizes the answers to these two questions. Since the answers to these questions merely indicate an opinion, the data must be accepted with caution. However, these data substantiate the figures in table 8 and indicate that the majority of operations in North Carolina are done for convenience and socioeconomic indications.

Each hospital also was asked whether it had a written list of requirements for tubal ligation, and, if so, to send a copy of these requirements. Twenty-one, or 30 per cent, of the hospitals performing sterilizations had written bylaws covering the procedure. The hospital bylaws concerning sterilization are summarized in table 10.

Table 8

Summary of Indications for 70 Hospitals Performing Tubal Ligations

Distribution by Hospitals According to Number of Deliveries	Per Cent	Age	Per Cent	Parity	Per Cent
Hospitals with less than 250 deliveries	11	No specific requirement	69	No specific requirement	15
Hospitals with 251-500 deliveries	29	Minimum age for tubal ligation 30 and above	31	Parity of 3 or more	13
Hospitals with 501-1,000 deliveries	34			4 or more	42
Hospitals with more than 1,000 deliveries	26			Parity of 5 or more	24
				operation performed only for medical considerations	6

Table 9

Answers to Questions Concering Tubal Ligation*

Answers According to No. Hospital Deliveries	Question 1 Yes	Question 1 No	Question 2 Yes	Question 2 No	Answers According to the Incidence of tubal ligation	Question 1 Yes	Question 1 No	Question 2 Yes	Question 2 No
Hospitals with less than 250 deliveries	15%	85%	50%	50%	Ligations 1:10-20 deliveries	55%	45%	18%	82%
Hospitals with 251-500 deliveries	50	50	30	70	Ligations 1:21-35 deliveries	69	31	13	87
Hospitals with 501-1,000 deliveries	74	26	32	68	Ligations 1:36-55 deliveries	50	50	33	67
Hospitals with more than 1,000 deliveries	38	62	30	70	Ligations 1:over 55	23	77	40	54

*Questions

1. In your hospital, are minor medical problems used as indications for tubal ligation when the operation is actually performed for conveniences or socio-economic indications?
2. In your hospital, are tubal ligations performed only for major medical indications?

Table 10

Summary of Written Hospital By-Laws Regarding Sterilization

Written rule	No. Hospitals
Approval by sterilization committee	4
Approval by Sterilization committee; 4 living children	3
Indications for sterilization, Donnelly and Lock: North Carolina J. Med. 14-1, 1953	3
Approval by 2 consultants	1
Age 30, 3 living children; below age 30, approval by 3 consultants	1
Age 30, 3 living children; 4 living children regardless of maternal age	1
5 living children, approval by 2 consultants	1
Parity of 6; approval by 2 consultants	2
Age 35, 3 living children	3
Age 30, 4 living children	2
Below 30, 5 living children	
Medical indications only	
Total	21
	(30% of hospitals performing sterilizations and reporting)

It is evident that there is little consistency in the written requirements for tubal ligation among the hospitals in this state. In three hospitals, however, clear and definitive indications for tubal ligation concerning age and parity were given. These may be summarized as follows: Tubal ligations are permitted on patients who are 35 or more years of age if they have three living children. Patients who are 30 and older may have tubal ligations if they have 4 living children. Patients who are below the age of 30 must have 5 living children before tubal ligation is allowed.

Correlation of the Per Capita Buying Power of a County and the Incidence of Tubal Ligation

In an effort to determine if there was any correlation between the socioeconomic status of a county and its incidence of tubal ligation, figure 1 was prepared. Data

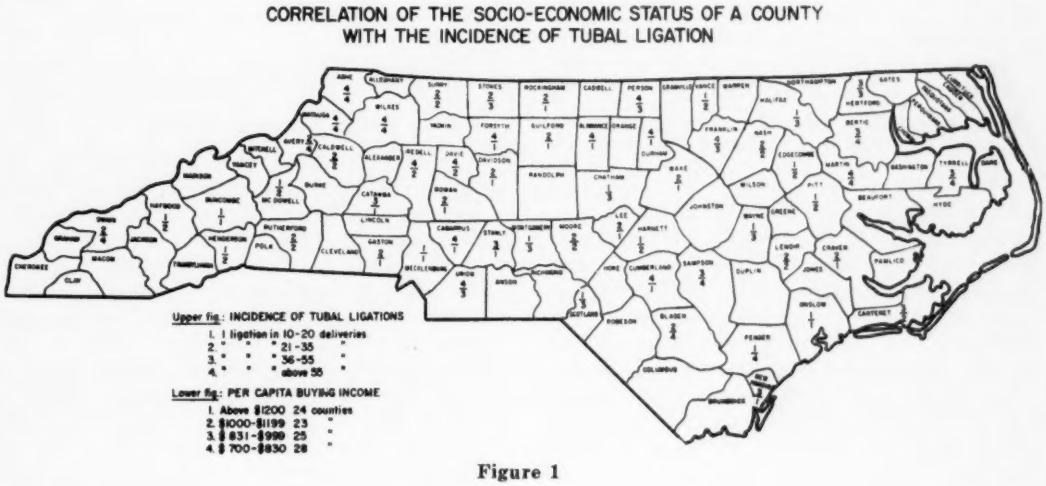
CORRELATION OF THE SOCIO-ECONOMIC STATUS OF A COUNTY
WITH THE INCIDENCE OF TUBAL LIGATION
Upper fig.: INCIDENCE OF TUBAL LIGATIONS
1. 1 ligation in 10-20 deliveries
2. " " " 21-35 "
3. " " " 36-55 "
4. " " " above 55 "
Lower fig.: PER CAPITA BUYING INCOME
1. Above $1200 24 counties
2. $1000-$1199 23 "
3. $ 831-$999 25 "
4. $ 700-$830 28 "

Figure 1

Table 11

Correlation of the Incidence of Tubal Ligation with Race, Perinatal Mortality and Socioeconomic Index in Hospitals Having Less Than 250 Deliveries Per Year

County	Deliveries			% Deliveries		Incidence of Ligation			Perinatal Mortality	Socio-Economic Index
	Total	White	Non-white	White	Non-white	Total	White	Non-white		
Carteret	243	243	0	100	0	1:61	1:61	0	16.5	2
Cumberland	723	634	89	88	12	1:16	1:15	1:44	34.6	1
Davie	493	409	84	83	17	1:82	1:81	1:84	28.3	2
Henderson	183	160	23	87	13	1:10	1:11	1:6	32.8	2
Halifax	342	126	216	37	63	1:10			52.6	3
Martin	521	412	109	79	21	1:88			46.1	4
Stoker	673	530	143	79	21	1:29			26.7	3
Swain	604	558	46	92	8	1:17	1:16		21.5	4
Watauga	149	149	0	100	0	1:49	1:49		40.5	4

Table 12

Correlation of the Incidence of Tubal Ligations with Race, Perinatal Mortality and Socioeconomic Index in Hospitals Having 251 to 500 Deliveries Per Year

County	Deliveries			% Deliveries		Incidence of Ligation			Perinatal Mortality	Socio-Economic Index
	Total	White	Non-white	White	Non-white	Total	White	Non-white		
Ashe	1262	1243	19	98	2	1:97	1:95		31.7	4
Bertie	1120	405	715	36	64	1:36			64.3	4
Bladen	1403	776	627	55	45	1:19			44.9	4
Caldwell	1322	999	323	76	24	1:27			33.3	2
Craven	916	1	915	0.2	99.2	1:22		1:22	91:7	1
Durham	1426	1	1425	0.1	99.9	1:57			61.0	1
Edgecome	1016	630	386	62	38	1:13	1:13	1:13	57.1	2
Franklin	1086	605	481	56	44	1:57			61.7	3
Gaston	1235	0	1235	0	100	1:17		1:17	55.1	1
Lenoir	1472	1129	343	76	24	1:52			60.5	2
Pender	983	513	470	52	48	1:12	1:16	1:9	42.7	4
Pitt	1458	483	975	33	67	1:21	1:24	1:19	31.6	2
Vance	791	0	791	0	100	1:16		1:16	55.6	2
Vance	1266	1265	1	99.9	0.1	1:26	1:26		26.1	2
Wake	1146	1143	3	99.7	0.3	1:41	1:41		34.9	1
Watauga	1032	1016	16	98	2	1:61	1:60		35.9	4

are presented for each county which answered the questionnaire.

The top figure of the fraction in each county represents the incidence of tubal ligation in that county. The incidence is divided into four essentially equal divisions according to the percentage distribution of table 7. The bottom figure of the fraction is a socioeconomic index based upon a sales management survey of buying power[2]. The buying power of the counties of North Carolina is broken into four equal divisions as indicated on the bottom of the map.

It is evident that there is no consistent distribution of the incidence of tubal ligation according to the Coastal, Piedmont, or Mountain counties of the state. Moreover, it is evident that there is no consistent correlation between the incidence of tubal ligation and the socioeconomic index of the county. Mecklenburg and Buncombe Counties, which have the highest per capita buying power, also are in the group of the hospitals with the highest incidence of tubal ligation. Many counties have no correlation between the incidence of tubal ligation and their socioeconomic index. There are a number counties, however which have a fraction of 4 over 1 and 1 over 4. Counties with these fractions are carrying out at least a consistent and possibly a realistic program of tubal ligation ccording to the socioeconomic conditions in their counties.

Correlation of the Incidence of Tubal Ligation with Race, Perinatal Mortality, and the Socio-Economic Index of a County

Tables 11, 12, 13, and 14 attempt to correlate the incidence of tubal ligation with pernatal mortality and with socioeconomic conditions as determined by the utilization of per capita buying income. The hospitals are divided into the four major divisions according to the number of deliveries each year. Representative data are given for each division. These four tables indicate that there is no consistent correlation between the incidence of tubal ligation and race, perinatal mortality, and socioeconomic status. In some hospitals, there is a cor-

Table 13

Correlation of the Incidence of Tubal Ligations with Race, Perinatal Mortality, and Socioeconomic Index in Hospitals Having 501 to 1000 Deliveries Per Year

County	Deliveries			% Deliveries		Incidence of Ligation			Perinatal	Socio-Economic
	Total	White	Non-white	White	Non-white	Total	White	Non-white	Mortality	Index
Catawba	1726	1527	199	88	12	1:45			29	1
Columbus	2318	1608	710	70	30	1:66			39.7	3
Halifax	2269	1397	872	62	34	1:9	1:13	1:6	60.8	3
Harnett	1841	1268	573	69	31	1:17	1:14	1:31	55.9	2
Haywood	2549	2489	60	98	2	1:11			23.1	2
Hertford	1757	939	818	53	46	1:43	1:94	1:26	27.9	3
Lee	2642	1862	780	70	30	1:30			42.0	1
Lenoir	2996	2287	709	76	24	1:39	1:47	1:25	38.7	2
McDowell	2157	2020	137	94	6	1:15	1:14	1:68	29.7	2
Moore	2144	1515	629	71	29	1:32	1:38	1:23	35.9	2
Nash	2388	1927	461	81	19	1:12	1:18	1:5	47.3	2
New Hanover	1581	1	1580	0.1	99.9	1:36		1:36	72.7	1
Pitt	2443	1724	719	71	29	1:12	1:27	1:5	45.8	2
Sampson	1831	1366	465	75	25	1:54	1:47	1:93	37.1	4
Union	2693	2257	382	84	16	1:57	1:64	1:31	39	3
Wake	2319	2	2317	0.1	99.9	1:47		1:47	65.5	1
Wilkes	2102	1956	146	93	7	1:105	1:108	1:73	31.9	4

relation between the incidence of ligation and the number of Negro deliveries and the perinatal mortality. In other counties, there is no such correlation.

In table 11, it is seen that in a Henderson County hospital the incidence of tubal ligation is 1 in 10 deliveries. Among white patients, however, it is 1:11, and among non-white patients 1:6. This represents a consistent practice, However, the reverse is true in a small hospital in Cumberland County where the incidence of ligation is 1:16 for the entire hospital, 1:15 for white and 1:44 for non-white. There is no correlation between the high incidence of tubal ligation in this hospital with the other hospitals in the county and the socioeconomic index of this county. On the other hand a hospital in Edgecombe County has an incidence of tubal ligation for the entire hospital of 1:13, and there is a similar incidence for white and non-white patients. Pitt and Pender Counties have a higher incidence of tubal ligation among the non-white than the white patients. On the other hand, in table 13 it is evident that the reverse is true in Halifax, McDowell, and Sampson Counties, where the incidence of tubal ligation is lower among the non-white patients than among white patients. Non-white patients in these counties are either resistant to the procedure or it is not offered to them.

Table 14 presents data from hospitals having 1,000 deliveries or more per year. These hospitals have, in general, the lowest perinatal mortality, the highest socioeconomic index, and also some of the highest incidence rates of tubal ligation. Thus,

Table 14

Correlation of the Incidence of Tubal Ligation with Race, Perinatal Mortality, and Socioeconomic Index in Hospitals Having More Than 1000 Deliveries Per Year

County	Deliveries			% Deliveries		Incidence of Ligation			Perinatal	Socio-Economic
	Total	White	Non-white	White	Non-white	Total	White	Non-white	Mortality	Index
Alamance	4933	4141	792	84	16	1:69	1:106	1:24	28.4	1
Buncombe	4749	3953	796	83	17	1:13	1:12	1:17	37.3	1
Cabarrus	478	3804	976	80	20	1:165	1:173	1:139	30.5	1
Forsyth	5838	5834	4	99.9	0.1	1:80	1:80		29.6	1
Forsyth	5294	5294	0	100	0	1:56	1:56		36.3	1
Gaston	4028	4027	0	100	0	1:23	1:23		28.3	1
Guilford	5575	5566	9	99.8	0.2	1:34	1:34		28.3	1
Guilford	5703	4876	827	85	15	1:74	1:77	1:55	34.5	1
Mecklenburg	5806	5803	3	99.9	0.1	1:25	1:25		29.3	1
Mecklenburg	4976	4972	4	99.9	0.1	1:22	1:22		28.1	1
Rockingham	3222	2234	988	69	31	1:30	1:33	1:25	32.3	1
Rowan	4419	3418	1001	77	23	1:24	1:25	1:22	31.9	1
Wake	6240	6238	2	99.9	0.1	1:27	1:27		34.8	1
Wayne	3430	2463	967	72	18	1:20			43.1	3

Table 15-A

Summary of Maternal Deaths Resulting From Tubal Ligation

Year	Race	Age	Parity at Time of Death	Indication for Operation	Day of Ligation	Obstetric Complications	Appendectomy	Postoperative Complications	Cause of Death
1949	W	28	4	Severe asthma	3	None	No	Intestinal obstruction at site of ligation	Intestinal Obstruction
1949	W	21	2	Severe toxemia	2	Severe toxemia Delivery macerated Stillborn	No	Intestinal obstruction, pelvic peritonitis	Pelvic infection 60 days postop.
1949	C	29	8	Toxemia and parity	5	Severe toxemia pulmonary edema 2½ weeks prior to delivery	Yes	Wound disruption 10th day	Pulmonary embolus 33 days postop.
1950	C	36	11	Toxemia and parity	4	Severe toxemia of pregnancy twins	No	Wound disruption 7 days postop.	Pulmonary emboli 11 days postop.
1950	W	27	3	Rheumatic heart disease with failure	3	Induction of labor because of decompensation. Ligation performed despite decompensation and anemia	No	Pulmonary emboli	Pulmonary Emboli 60 days postop.
1950	C	27	3	Epilepsy	1	None	No	None	Autopsy findings compatible with eclampsia death 30 hrs. postop.

in many of these hospitals where good obstetrics is practiced, tubal ligations are performed solely for the convenience of patients.

Six of the 70 reporting hospitals which perform tubal ligation were limited to Negro patients. These hospitals had 7,972 deliveries and 272 ligations. Thus, the incidence among the Negro hospitals was 1:29, which is essentially the same as the incidence among the entire sample. Two of these hospitals fell in the group having an incidence of 1:21-35, while there was one each in the lower incidence groups.

Maternal Mortality Resulting from Tubal Ligation

Table 15 gives the maternal deaths which have been reported to the Maternal Mortality Committee from 1946 to 1958. Thirteen deaths were caused by tubal ligation. Three maternal deaths attributed to tubal ligation occurred during the three years which have been surveyed. The data from this study indicate that approximately 8,645 tubal ligations were performed in North Carolina in the three years 1955, 1956, and 1957. Since there were 3 deaths in 8,645 tubal ligations, the maternal mortality was 1:2882 operations. This ratio is somewhat lower than that reported by Prystowsky and Eastman[3].

It is apparent on reviewing this date that the majority of these deaths occurred in women who had severe obstetric complications or severe varicosities. This finding would indicate that puerperal sterilization is a reasonably safe procedure in the uncomplicated obstetric patient, but when there are severe medical or obstetric complications an interval ligation or hysterectomy would be preferable to a puerperal ligation. This would seem true even if a pregnancy had to be interrupted at the time of the ligation, since in many cases life expectancy may be curtailed by an additional pregnancy.

It is also evident that ligations were delayed from three to five days in 8 of the cases. It is believed that a puerperal ligation should be performed within the first 24 hours after delivery, and it should not be accompanied by an appendectomy.

The Legality of Sterilization in North Carolina

Broadway[4] has concisely summarized the legality of sterilization in North Carolina:

> Involuntary sterilization of the insane or mentally deficient is provided for by a North Carolina statute after the case has received the approval of the Eugenics Board. Those partici-

Table 15-B

Year	Race	Age	Parity at Time of Parity	Indication for Operation	Day of Ligation	Obstetric Complications	Appendectomy	Postoperative Complications	Cause of Death
1952	W	21	3	Elective	1	Prolonged labor, Pituitrin stimulation, low forceps	Yes	None	Pulmonary embolus 7 days postop.
1953	W	38	9	Parity of 8 Pt. Deaf and dumb, 2 children deaf and dumb	1	None	No	None	Pulmonary embolus 5 days postop.
1954	C	27	6	Severe varicosities	5	None	No	Pulmonary emboli	Pulmonary embolus 5 days postop.
1954	W	37	7	Severe varicose veins Asthma	5	Obesity Puerperal infection with thrombophlebitis prior to operation	No	None	Pulmonary Embolus 14 days postop.
1955	C	31	2	Severe diabetes Previous eclampsia	120	Diabetes Toxemia	No	Pelvic abscess 11 Days P.O.	Septicemia 11 days postop.
1955	W	37	6	Elective	5	None	No	Pulmonary emboli 3rd P.O. Day	Pulmonary embolus 7th P.O. day
1956	C	37	8	Chronic hyperensive disease	3	Refused interruption of pregnancy B.P. 210/116, 3 † albuminuria, Induction of labor Premature Separation of placenta	No	None	Cerebral vascular accident 4 days P.O.

pating in the procedure are exempted from liability except in case of negligence.

No other law affecting sterilization appears on the North Carolina statute books. Those who have studied the subject believe that a doctor may protect himself from financial liability in cases of voluntary sterilization by the use of a properly drawn release or contract. They also believe that there is no criminal liability on the ground that sterilization might be considered to be mayhem. No case bearing directly on this matter has been tried in the North Carolina courts.

Thus criminal liability on a basis of mayhem is improbable, but it is still theoretically possible under the present negative statutes.

During the years 1955-1957, 644 sterilizations were performed with the approval of the Eugenics Board. This represents 7.4 per cent of all of the sterilizations in the state for these years. On the other hand, 92.6 per cent of the sterilizations did not have Eugenics Board approval and were not directly covered by North Carolina statutes.

Summary and Conclusions

A study of tubal ligations in North Carolina has been made for the years 1955, 1956, and 1957. This study covered 169,272 deliveries and 5,209 tubal ligations. From the data obtained one may assume that 2,880 tubal ligations are performed in North Carolina each year, with an incidence of one ligation in every 32 deliveries.

Seventy-five per cent of these operations were performed for the convenience of the patient or for socio-economic indications; 7.4 per cent were performed with the approval of the Eugenics Board.

No consistent correlation was found between the incidence of tubal ligation and the number of hospital deliveries, race, per capita buying power, perinatal mortality, or geographic location in the state. Only 30 per cent of those hospitals performing tubal ligations had written rules concerning the procedure. Some hospitals presented a well delineated practice of tubal

ligation based on the socio-economic needs of their counties. In other hospitals, tubal ligations were performed for the convenience of the patient.

It would seem advisable for each county medical society to study the practice of tubal ligation in their county and adopt basic written rules for the procedure.

It would also seem reasonable for the Legislative Committee of the State Medical Society and the Society Attorneys to study the practice of tubal ligation in North Carolina and make appropriate recommendations to the Legislature in order that the legality of the procedure can be clarified. A properly drawn statute concerning voluntary sterilization would be of help to both physician and patient.

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Discussion

Dr. Jesse Caldwell (Gastonia): The presentation you have just heard should become a classic record. To my knowledge there is no comparable resume of experience available to us at this time.

The authors have compiled a tremendous amount of material from many sources, most of which are not readily available to the profession in general. Thus we are given a reflection of what we have done in the past decade regarding sterilization of the female human being.

Such a compilation is absolutely necessary if we are to evaluate a procedure which is now our privilege to perform under our medical and surgical franchise.

The marked variation in the indications for puerperal sterilization indicates a corresponding variation in the attitude of the medical mind concerning the procedure. However, his variation in attitude is not limited to operative sterilization. An analysis of tonsillectomies or appendectomies would probably show similar results.

The chart showing the maternal deaths resulting from tubal ligation is a unique document, and should be studied carefully and thoughtfully by all of us who recommend or perform operative sterilization. The fact that pulmonary embolus was found to be the most frequent cause of death, and often in patients who had severe obstetrical complications, raises the question as to whether the puerperium is the ideal time for the operation in complicated cases. Of course, this incidence should be compared with that of fatal emboli associated with obstetric complications following delivery without tubal ligation. The same goes for tubal ligations done for elective or minor indications.

Puerperal tubal ligation is a popular operation. Many of our vivacious patients look forward to qualifying for sterilization, on the basis of multiparity, with the same excitement and enthusiasm that they did toward their graduation or engagement. Another milestone has been reached, and they reason that they are entitled to stop worrying about conception. Given this type of patient and a considerate and obliging physician, you have a combination which is successful, in some way or other, in overcoming such obstacles as consultants, age, parity, and the absence of major indications.

Periodic examination of the obstetric records of almost any hospital will uncover a large number of patients who needed the benefit of sterilization but who have been discharged without hearing the subject mentioned to them. The records of patients with severe hypertension, chronic renal disease, diabetes, and some with Rh iso-immunization cases, who are discharged without sterilization, should carry a notation that this procedure was considered, and reasons should be given why it was not done. In other words, many patients who need the operation are not getting it, while others who do not need it are getting it.

It is doubtful if uniform indications for tubal ligation can be agreed upon at this time. Meanwhile, the next most desirable thing is to have more presentations similar to the one just given by Drs. Flowers, Burwell and Donnelly.

Dr. O. Hunter Jones (Charlotte): In March I received a request from Dr. C. E. Flowers for statistics on tubal ligations done at Charlotte Memorial Hospital. It seems that two letters to the administration of the hospital had failed to produce the figures. Thereupon, Dr. Donnelly suggested to Dr. Flowers that I would obtain the figures for him, but also warned him to expect a "long letter" in addition. He was right. Here is the "long letter" to Dr. Flowers:

"You didn't ask for my comment; nevertheless, I am not going to let this opportunity go by without expressing myself. Frankly, I do not know the answer to the sterilization problem. I agree with the Editor of the Year Book of Obstetrics and Gynecology for 1956-1957 when he said 'sterilization for medical indications is being done less and less, but the number of sterilizations for economic reasons and psychiatric indications is increasing.'

"I am becoming more convinced every year that sterilization for multiparity should not be 'frowned upon,' as it is. It seems to me that it boils down, basically, to the question of what right does the patient and her husband have? I know of no reason why we should tell a couple that postpartum tubal ligation can be done after they have five children. Why does this couple have to have five instead of four children? Many obstetricians (including myself) have only three children, desire

no more, and could well wish that postpartum tubal ligation had been done after the third. Yet, this wouldn't be fair, because we would feel obligated to do the same for any patient, in similar circumstances, who requested it.

"I do not do very many sterilizations. However, when I think the request is reasonable, I do not hesitate to perform this operation. In one case it may be with the fifth pregnancy, with another it may be with the fourth. Offhand I cannot remember doing one with the third (except at cesarean section, or for a definite medical indication); however, I would not hesitate if I felt that the need existed. Of course I am quite aware of all the objections to tubal ligation. I have to go through this 'song and dance' every week with one or more patients to get out of doing the operation.

"The conscientious and honest obstetrician who has taken care of his patient for years probably is a far better judge of whether sterilization is reasonable than any departmental committee, any hospital committee, or any 'Brain Trust' on a state or national level. There is one thing that not even the 'Brain Trust' can change and that is human nature. Some people are not going to use contraception **all of the time!** Now the medical profession can accept this or not, just as it wishes, but it certainly cannot change it! Being 50 years of age, I believe that I have lived long enough to realize that a family of average intelligence, and of average income, will do more good for society having only the number of children they can properly rear. 'Making' a couple continue to bear children, against their will, is neither good for the couple nor for the child. I have asked patients many, many times, 'Why did you take a chance if you didn't want another baby?' The answer is always the same. You know it as well as I do. It simply boils down to the fact that you can't change human nature. Human nature is often careless.

"There is one question about sterilization that I would like for someone to answer. I am a Baptist. Now the Catholics have their own ideas about sterilization, but at least they are consistent. They are opposed to both contraception and sterilization. We Protestants, on the other hand, are all for contraception and planned pregnancies, but many argue against sterilization. Now I would like for some Protestant minister or theologian who has a good answer to tell the rest of us what is the Christian thing to do about sterilization.

"O. Hunter Jones, M.D."

Dr. John C. Burwell (Greensboro): From this study, two facts which do not admit of argument stand out. The problem of sterilization is not only statewide, but bears little or no relationship to race. When we recall that an average of 1 out of every 30 pregnancies is followed by operative sterilization, we are forced to admit that the situation is one which concerns all of us. These facts should be kept in mind in considering the broader implications of the facts presented.

North Carolina physicians face at least a sporadic bombardment of requests for surgical sterilization. It is undeniable that we have at times leaned over backwards to oblige these requests, even in the face of a lack of legal sanction. Varying administrative hospital regulations throughout the state ameliorate but do not solve the problem. And it is a very real problem.

With an increasingly complex social structure, the difficulties of feeding, clothing, and educating a large family become more and more pronounced. In seemingly ever greater numbers, families beg the doctor for a sure and lasting relief from the fear of future pregnancies. If we can find medical indications for the procedure, the solution is easy. If, however, as is frequently the case, no medical indications are present, we must either refuse or risk the displeasure of hospital governing boards and possible legal reprisals. We all know too well the consequences of refusal. Specialists and generalists alike have seen them time and time again. The woman who considers her family to be complete may either have experienced contraceptive failures or lack the confidence to employ contraception. Soon marital relations are overshadowed by the fear of pregnancy, and dyspareunia and frigidity all too frequently result. The regression of the wife to the status of a sexual recluse may send the husband to more receptive arms, and the groundwork for family disruption is laid. Somehow, family unity and stability would seem deserving of more consideration.

If, on the other hand, the doctor stretches a point and acquiesces to patient pressure for sterilization, both physician and patient are legally guilty of mayhem under our present state laws. This is wrong. Parents who assume responsibility for the financial support and education of their children deserve some voice in determining the number of these children. If family support is a family responsibility, family size should be a family prerogative.

In this state we not only enjoy the rights and liberties guaranteed under the constitution, but have gone even further to enact legislation insuring the right to work. By a curious discrepancy the family is denied the simple legal right of family limitation. It is my personal conviction that this Society should express itself as favoring this right.

Closing Remarks by Dr. Flowers

I am grateful for the interesting and thoughtful remarks of the discussants of this paper.

It is apparent that this complex problem is not going to be solved here today; indeed, it will be extremely difficult to establish state-wide rules concerning the practice of tubal ligation within the next five years. But county medical societies can

and should establish local ground rules for the procedure forthwith.

The fact that more than 2,800 tubal ligations are performed in North Carolina is neither surprising nor disturbing. But it is particularly painful to find that a hospitalization policy may be an influencing factor in a puerperal ligation. It is also disturbing to find that in some instances the privilege of tubal ligation is not extended equally to all patients despite their race or financial status.

It would seem that the County Medical Society in establishing its rules concerning tubal ligation should consider certain basic principles:

1. The rules should be written and included in the by-laws of the hospital.

2. Rules concerning age and parity should be specific but adjustable to the socio-economic conditions of the patient.

3. A sterilization committee should be appointed to decide cases not specifically covered in the by-laws.

4 Consultants should be used to decide medical and surgical issues, not indications for tubal ligations which concern only age and parity.

5. Interval ligations or hysterectomies should be performed when there are severe medical or obstetric complications or when the patient has severe varicosities.

6. Hysterectomies should be used in lieu of tubal ligations if there is vaginal relaxation or uterine disease.

7. Periodic audits should be made concerning the practice of tubal ligation in a hospital.

Finally our laws should be living laws that can be adjusted to the realities of the present and possibly to the logarithmic growth curve of the world population. If tubal ligations are going to be performed for convenience or socio-economic reasons, as indeed they are being performed in our state, it would seem that this operation should be covered by the North Carolina statutes. Thus patients who desire this procedure and physicians who employ it should use their prerogative of consulting their state senators and representatives, and should place this problem before the Legislative Committee of our State Medical Society.

My closing remarks reflect my own individual thoughts and opinions, not necessarily those of the other authors. Dr. Donnelly, Dr. Burwell, and I are grateful for the opportunity of presenting this material to the Section on Obstetrics and Gynecology of the North Carolina Medical Society.

E. D. Hutchinson has made interesting studies of creative insight in the great scientific and artistic geniuses of the past and present, such as Archimedes, Newton, Poincare, Einstein, Mozart, Coleridge and many others. A report of Hutchinson's work will be found in the journal, *Psychiatry*, during the period 1939-42. One outstanding thing about this creative phenomenon (the inductive leap, as they call it) is that although hard, intellectual work and struggle are prerequisites, the actual flash—the great discovery; the new thought—never comes at the peak of mental effort, but during moments of relaxation and leisure. This has been confirmed again and again—for instance, Poincare while boarding a streetcar, Newton under the apple tree, and Archimedes in the bathtub.—Martin, A. R., Recreational Measures and Their Value to Older People, J. Am. Geriatrics Soc. 7:531 (July) 1959.

Evaluation of Diagnostic Procedures In 100 Patients With Gastrointestinal Symptoms

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Cancer of the stomach accounted for 5.6 per cent of all cases of cancer reported in 1956. Of 24,000 patients with gastric cancer in this year, 22,119 died[1]. The need for methods of early detection is obvious.

Methods of Detecting Gastric Cancer

The incidence of gastric cancer increases sharply in men after the age of 45, and in women after 50. Individuals with pernicious anemia, atrophic gastritis, or gastric polyps seem predisposed to gastric cancer. In this group of patients the symptoms of early cancer may be few, or atypical and mild. Periodic observation and re-evaluation of such persons are essential prophylactic measures.

Determinations of gastric acidity

Determinations of the gastric acidity provide a valuable screening test. Probably more than 50 per cent of patients with gastric cancer are achlorhydric even after histamine stimulation, and many others have diminished acidity[2]. Hitchcock[3] has estimated the incidence of gastric cancer in patients with achlorhydria or hypochlorhydria to be more than five times greater than that in persons with normal acidity. The development of ion exchange techniques for determining gastric acidity without intubation should permit more widespread application of this valuable screening procedure[4].

Roentgen surveys

Mass roentgen surveys, even in selected age groups, have failed to disclose enough asymptomatic, resectable lesions to justify the amount of work involved, the time required of highly trained personnel, and the potential dangers of excess radiation through repeated examinations. Roentgen studies for the purpose of ruling out asymptomatic unsuspected gastric cancer seem justified only in patients with one of the predisposing conditions mentioned above—pernicious anemia, atrophic gastritis, gastric polyps, or achlorhydria.

Gastroscopy

Gastroscopy is of value primarily in making possible an unequivocal diagnosis of gastritis and in disclosing occasional lesions not shown by roentgen studies. It also permits more accurate diagnosis of lesions found by x-ray examination, and makes it possible to observe the effects of clinical management on gastric ulcerations of uncertain etiology.

Gastric cytology

While gastric lavage with cytologic study of the gastric contents is a time-consuming procedure requiring highly specialized technical assistance, this method may disclose the presence of malignant cells before a lesion could be detected by roentgenologic or gastroscopic examination.

Exfoliation of gastric cells is a normal physiologic process. Malignant cells, because of their lowered calcium content, friability and necrosis, lack of adhesiveness, and greater susceptibility to trauma, show an increased tendency to exfoliation.

A variety of methods for obtaining gastric cells have been described. They include mechanical abrasion with a brush or balloon, lavage using mucolytic enzymes, and simple lavage with Ringer's solution. The mechanical methods appear of particular value when a lesion in the antrum or fundus is suspected, or when simple lavage has proved unsatisfactory. Sheets of cells are usually obtained by mechanical abrasion, but the time required and the occa-

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sional untoward effect of passing balloons and brushes have discouraged the widespread use of these procedures.

Although attempts to liquefy the mucous layer in the stomach with crude enzyme mixtures do not regularly yield well preserved cells, some investigators[5] have reported favorably on the use of crystallized chymotrypsin. Saline lavage and aspiration, however, is the simplest and least traumatic procedure. In most instances adequately preserved cells are recovered in sufficient quantity to permit diagnostic evaluation[6]. In the study to be reported we have employed this method to obtain gastric washings for cytologic examination.

Selection of Patients for Cytologic Studies

One hundred patients were studied. These patients were selected because of symptoms referable to the gastrointestinal tract or findings suggesting gastric cancer. Cases of proven duodenal ulcer were excluded. The group included 61 men whose ages averaged 54.4 years and 39 women with an average age of 51.6 years.

Method of Examination

The patient was permitted to eat a light meal the night before the study, and water was allowed in unlimited amounts until bedtime. The following morning two separate lavages were performed on the fasting stomach. The first eliminates mucus and any debris. The second usually contains the best preserved exfoliated cells. A total of 300 cc. of saline solution was injected into the stomach by syringe and the fluid was barbotaged vigorously for three minutes, with frequent re-location of the gastric tube. All the solution that could then be aspirated was placed in 50 cc. centrifuge tubes immersed in ice. These were centrifuged immediately at 2700 rpm for ten minutes, the sediment was smeared on slides which were fixed in ether-alcohol.

During the second washing with an additional 300 cc. of saline solution the patient was rotated 90 degrees from back to side at two-minute intervals and the abdomen gently massaged. After a period of eight minutes the solution was aspirated and prepared in the manner described above.

Cytologic Classification

The cytologic specimens were classified as follows:

Class 0—Inadequate for diagnosis.

Table 1

Final Cytologic Classification of Gastric Washings from 100 Patients

	0	1	2	3	4
No. cases	8	40	35	12	5
Age range	38-71	28-72	28-78	28-82	51-68
Average age	64.2	50.5	57.4	59.8	57.2

Class 1—No atypical or abnormal cells.

Class 2—Atypical cells, but no evidence of malignancy.

Class 3—Cells suggestive of malignancy, but not conclusive.

Class 4—Cells strongly suggestive of malignancy.

Table 1 shows the number of cases coming under each classification, and the average age of the patients in each group. It will be seen that the average age of the patients with atypical and abnormal cells (classes 2-4) is slightly greater than that of the patients with normal cytology (class 1).

Pathologic Conditions Present in Patients Without Cytologic Evidence of Malignancy

Lymphosarcoma

Lymphosarcoma was diagnosed by surgical biopsy or at autopsy in 4 patients of this series (table 2), all of whom had negative cytologic examinations of gastric washings. This group of patients will be considered separately, since the cytologic diagnosis, therapy, and prognosis of gastric sarcoma or lymphosarcoma differ from those associated with adenocarcinoma.

In patient CRK laparotomy revealed a primary lymphosarcoma of the spleen, with extension to the stomach; the gastric mucosa, however, was not involved, and it is not surprising that both preoperative and postoperative cytologic examinations were negative.

Cytologic studies were also negative in patient LUB. The radiologic examination, however, suggested the correct diagnosis, and surgical biopsy revealed an infiltrative submucosal lymphosarcoma of the stomach. The gastric mucosa was intact.

Patient HR was not studied cytologically before gastric resection was performed for a recurrent ulcer on the lesser curvature. At operation, reticulum sarcoma cells were found in the borders of the ulcer. Cytologic examination of the gastric washings six months later, when the patient was asymptomatic, revealed cells resembling reticulo-

Table 2

Findings in Four Patients with Sarcoma or Lymphoma

	Age	Sex	Cytology Class Preop.	Postop.	Roentgen Findings	Final Diagnosis	Comment
CKR	52	M	2	1	Mass displacing greater curvature	Lymphosarcoma of spleen extending to stomach; mucosa not involved	Mass removed
LUB	68	F	2		Thick folds, ? lymphosarcoma	Infiltrative lymphosarcoma; mucosa intact (biopsy)	Enlarged nodes, liver, spleen
HR	45	M		2	Lesser curvature ulcer; recurrence 2 mos. later	Reticulum cell sarcoma; cells found in ulcer border.	Resection 6 mos. before cytology.
CH	62	M	2	No surgery	Normal G.I. series	Lymphosarcoma not involving G.I. tract	Postmortem examination

endothelial cells but showing no features diagnostic of malignancy. The presence of these cells probably indicated that the lesion had recurred, and roentgen therapy was administered despite the fact that the patient was asymptomatic and that radiologic examination of the stomach revealed a normally functioning gastroenterostomy.

Postmortem examination of CH revealed a Hodgkin's sarcoma. The gastrointestinal tract was not involved, although gastrointestinal symptoms were present.

Although conclusions drawn from this admittedly small group of patients may not be valid, it would appear that roentgen examination is more valuable than cytologic studies in the diagnosis of infiltrating submucosal gastric tumors such as lymphosarcomas.

Gastric ulcers

Cytologic examinations were done in 13 patients having roentgen evidence of gastric ulcers. Nine of these showed no cytologic evidence of malignancy (table 3), although two of the specimens were classified as inadequate for diagnosis. Both of these patients (CKA and TCC) had pyloric obstruction, with retention of food and secretions. In both cases the roentgen examination was suggestive of malignancy, but in patient CKA (fig. 1) the lesion was found at surgery to be benign. Necrotic debris in the ulcer itself, inflammatory cells, and retention of secretions contributed to the unsatisfactory specimens. In patient TCC the roentgen impression of a malignant ulcer was confirmed by exploration.

Roentgen evidence of malignancy was also present in patients CP and JC, both of whom had negative cytologic studies. Operation confirmed the presence of a benign ulcer in CP, but no follow-up was obtained

Table 3

Findings in Nine Patients with Gastric Ulcers and Negative Gastric Washings (Cytology Class 0, 1 or 2)

	Age	Sex	Free HCl	Cytology Class	Roentgen Findings	Gastroscopic Findings	Operative Findings	Follow-up
CKA	48	F		0	Malignant mass on greater curvature	Unsuccessful	Giant ulcer, benign	Asymptomatic following resection
TCC	61	M	0	0	Lesser curvature ulcer, ? malignant	Food and secretion	Gastric ca. with partial obstruction	
CP	69	M	†	2	Lesser curvature ulcer, malignant	Large mass, malignant	Benign ulcer perforating into pancreas	
JC	70	M	†	2	Lesser curvature ulcer, ? malignant	Not done		No follow-up
LFS	32	M	†	1	Lesser curvature ulcer, benign	Benign ulcer		X-ray neg. in 3 mos.
LJ	40	M	†	1	Lesser curvature ulcer, benign	Not done		No follow-up
JRP	55	M	†	1	Antral ulcer, benign; bezoar	Bezoar	Bleeding ulcer, bezoar	X-ray neg. 4 mos. after resection.
CJW	58	M	†	2	Antral ulcer, benign	Not done		Ulcer healing shown by x-ray 2 wks. later
JT	67	M	†	2	Lesser curvature ulcer, benign	Not done		X-ray neg. 10 mos. later

Fig. 1. (Patient C.K.A.) Large defect of the pars media considered as probably malignant. At operation a benign giant ulceration was resected. Retained secretions and food particles with necrotic debris from the lesion resulted in an unsatisfactory specimen in this patient.

in JC. In the remaining 6 patients with gastric ulcers, both cytologic and radiographic examinations were negative for malignancy.

Pathologic Conditions Present in Patients with Postive Cytology (Classes 3 and 4)

Eighteen patients had cytologic specimens suggestive of malignancy; 13 of these were diagnosed as class 3, and 5 as class 4.

Gastric ulcers and gastritis

Three patients with gastric ulcers had cytologic specimens classified as 3 or 4 (table 4). In patients JR and FL, however, repeat examinations were interpreted as class 2, and both were removed from the group classified as malignant. Because of the repeated absence of free acid after histamine stimulation and failure of the lesion to show healing after two weeks of therapy (figs. 2 and 3), JR had a subtotal gastric resection. The cytologic diagnosis of benignancy was confirmed by pathologic study of the resected lesion. Repeat x-ray examination of patient FL after two weeks of therapy showed healing of his ulcer. Three months later, follow-up roentgenologic and cytologic examinations were normal.

In patient HG a malignant ulcer of the greater curvature was suspected radiographically, and only one cytologic examination was made prior to operation; this was graded as class 3. Laparotomy revealed diffuse gastric bleeding without ulceration, and resection was not done. This patient gradually improved and has had no recurrence of symptoms.

A roentgen diagnosis of probable mass and ulcer in the cardia was made in patient ALM (fig. 4). Cytologic examination of the gastric washings revealed malignant squamous cells, class 4. At operation the patient was found to have a malignant mass involving the cardio-esophageal junction, and diffuse abdominal carcinomatosis.

These 13 cases of gastric ulcer indicate that gastric cytology is a valuable adjunct in the differential diagnosis of ulcerating gastric lesions. Although suspicious specimens were obtained in 3 cases, there were no false negatives. If a patient with a gastric ulcer has a negative cytologic specimen

Table 4

Findings in Four Patients with Gastric Ulcers and Suspicious or Positive Gastric Washings (Cytology Class 3 or 4)

	Age	Sex	Free HCl	Cytology Class	Roentgen Findings	Gastroscopic Findings	Operative Findings	Comment
JR	50	M	0	3, 2	Lesser curvature ulcer, ? malignant	Not done	Benign ulcer	Second cytologic exam. 5 days after the first was neg. in pts. JR and FL.
FL	54	M	†	3, 2	Lesser curvature ulcer, benign	Not done	No surgery	Healing complete in 3 mos.
HG	55	M		3	Greater curvature ulcer, ? malignant	Benign ulcer	No ulcer but diffuse bleeding (gastritis)	Not resected; gradual improvement
ALM	59	F	†	4	? Mass, cardia; ? ulcer, cardia	Not done	Carcinomatosis	Cytologic studies showed squamous ca. cells

Fig. 2. (Patient J.R.) Initial x-ray examination showing lesser curvature gastric ulcer.

Fig. 3. Repeat examination after three weeks of therapy. Gastric ulcer still present with little evidence of healing.

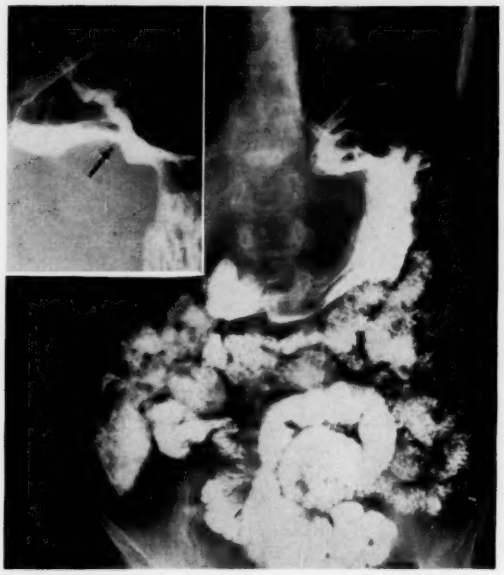

Fig. 4. (Patient A.L.M.) Displacement of esophagus at the cardio-esophageal junction. Insert shows probable ulceration, and mass lesion involving the lesser gastric curvature.

(class 1 or 2) and free hydrochloric acid, it may be assumed that his lesion is benign. Because atypical cells are often present during the healing phase of benign gastric ulcer, a cytologic examination which falls in class 3 should be repeated and interpreted in the light of other clinical findings. Class 4 cytology, however, should have the diagnostic implication of a positive surgical biopsy.

Gastric or esophageal carcinoma

Eight patients had gastric carcinoma diagnosed clinically or by surgical biopsy. In one of these (CWS) a false negative cytologic examination (class 2) was obtained preoperatively, although repeat examination six months after resection showed malignant cells (class 3) in the gastric washings. This patient had a linitis plastica type of infiltrative mucinous adenocarcinoma, which did not involve the surface layers of the gastric mucosa. In this case abrasive techniques of gastric lavage might have permitted the diagnosis to be made preoperatively.

In one patient (WHH) gastric washings obtained 16 months after gastric resection for cancer showed malignant columnar epithelial cells (class 4), although *preoperative cytology had been negative.* The patient was asymptomatic at the time of the second study.

Table 5

Findings in Nine Patients with Gastric or Esophageal Cancer

	Age	Sex	Free HCl	Cytology Class.	Roentgen Findings	Clinical Diagnosis	Operative Findings	Comment
EC	74	F		3	Constricting esophageal lesion	Esophageal cancer	Biopsy: esophageal carcinoma	Symptomatic improvement after radiation therapy
JRP	56	M		3	"Ulcer"	Gastric cancer	Carcinomatosis	Cytology revealed malignant columnar cells
MLS	60	F		3	Not done; gastroscopy showed large ant. wall mass	Gastric cancer		Large liver; alkaline phosphatase 20.3 B.u.
PHL	80	F	0	3	Mass lesion, middle third	Gastric cancer	Inoperable	Large liver; alkaline phosphatase 27.0 B.u.
CJ	82	M		3	Constriction, distal 2/3	Gastric cancer	Refused surgery	
CWS	52	M	†	2, 3	Deformity, lesser curvature	Gastric cancer	Mucinous adenocarcinoma, not involving the mucosa	Preoperative cytology 2; cytology 6 mos. after operation 3
WHH	53	M	0	1, 4	Not done	Gastric cancer (?)	Gastric cancer involving mucosa	Preop. cytology 1; cytology 16 mos. after resection 4; pt. asymptomatic
OC	68	M		4	Fixed contour, polypoid mass	Gastric cancer	Inoperable	Alkaline phosphatase 31 B.u.
RGS	55	M		4	Constricted distal third	Gastric cancer	Carcinomatosis	

In 4 additional patients with gastric cancer, cytologic examinations of gastric washings were graded as class 3, and in 2 as class 4. One patient (EC) with roentgen evidence of esophageal cancer (fig. 5) had a cytologic specimen diagnosed as class 3.

Pyloric channel ulcer

A cytologic classification of 3 was made on gastric washings from JRW, a 64 year old man with symptoms of anorexia, vomiting, and weight loss, and a diagnosis of channel ulcer was suggested by the roentgen findings. After two months of ulcer therapy the patient was asymptomatic, and roentgenologic and cytologic studies were negative. It is assumed that the suggestive cells seen initially in the gastric washings represented active proliferating cells from the channel ulcer.

Ulcerative colitis

JS, a 51 year old man with ulcerative colitis, represents the most difficult clinical problem precipitated by the study thus far. This patient has no upper gastrointestinal symptoms, and roentgen examination of the upper gastrointestinal tract has been negative. One cytologic examination, however, revealed malignant cells of the class 4 type, and repeat examination revealed a class 3 cytology.

Fig. 5 (Patient E.C.) The distal third of the esophagus and the cardia of the stomach involved by neoplastic mass.

Table 6

Other Pathologic Conditions Present in Patients with Positive Gastric Washings (Class 3 or 4)

	Age	Sex	Free HCl	Cytology Class.	Roentgen Findings	Clinical Diagnosis	Operative Findings	Comment
ADA	43	M		3	Negative	Functional G.I. disturbance		Unchanged after 4 mos.; cytology not repeated
MNP	60	F		3	Not done	Postnecrotic cirrhosis		Ascites, enlarged liver, pleural effusion; no follow-up (?)
PH	28	F	0	3, 3	Gastroenterostomy	? Marginal ulcer; anorexia nervosa	Duodenal ulcer found 1 yr. previously	Repeat cytology 3; no follow-up
JRW	64	M	†	3, 2	Channel ulcer	Channel ulcer		Good response after 2 mos. of therapy; repeat cytology 2
JS	51	M		4, 3	Negative	Ulcerative colitis		No upper G.I. symptoms. Repeat cytology 3

Undiagnosed cases

As might be expected, most of the diagnostic problems were in the patients with class 3 cytologic specimens (table 6). In one patient (ADA) a tentative diagnosis of functional digestive difficulty has been made. Patient MNP has had ascites, enlarged liver and pleural effusion for one year—findings which might well be due to gastric cancer, although the diagnosis in her case was postnecrotic cirrhosis.

Patient PH represents a particularly difficult problem. She lost 100 pounds in one year following a subtotal gastric resection for duodenal ulcer. The repeated finding of a class 3 cytology in spite of normal roentgen examinations of the upper gastrointestinal tract suggests that the patient may have an ulcer of the gastric pouch. Another exploratory operation is being considered.

Summary

1. Cytologic studies of gastric washings were made in 100 patients with gastrointestinal symptoms or other findings suggesting gastric lesions.

2. The cytologic findings were of no diagnostic value in 2 patients with lymphomas producing infiltrative, non-ulcerating submucosal gastric tumors.

3. A definite diagnosis of cancer has been made in 4 of the 5 patients with a class 4 cytology; in the fifth case, a patient with ulcerative colitis, the diagnosis is still in doubt.

4. Class 3 cytology has occurred in patients with cancer and in patients with benign healing ulcers or gastritis. Repeat examination has clarified the majority of these problems.

5. One false negative occurred in a patient with a submucosal gastric cancer.

6. In 2 patients, asymptomatic following resections for gastric cancer, cytologic examinations six and sixteen months postoperatively indicate recurrence of the malignant lesions.

Conclusion

Gastric cytology is a valuable adjunct in the diagnosis of gastric cancer and in the differentiation of ulcerating gastric lesions. Routine postoperative cytologic studies may also prove to be of value in indicating recurrences in asymptomatic patients.

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One Year's Experience With Staphylococcal Wound Infections on the Orthopedic Service Of a General Hospital

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The hospital from which these data were compiled is a 385-bed general hospital, operating at capacity census most of the time. Its patients encompass a cross section of the local white population.

The attending staff represents all the major specialties, and there is an intern and resident house staff. The admissions are predominantly private patients, and of the orthopedic admissions less than 10 per cent are medically indigent patients.

Over the past few years, in company with most other institutions throughout the world[1], this hospital has noted an increase in postoperative wound infections. This fact stimulated the formation of an infections control committee which has studied the hospital and made recommendations relative to housekeeping, aseptic and antiseptic techniques, and the physical plant. The orthopedic service, independently and in company with other services, has instituted an active program of study and control of surgical infections. This analysis of the surgical infections on the orthopedic service is presented as a part of that program.

The 86 orthopedic service beds are located on one floor of the hospital. In addition, orthopedic patients usually occupy three to six pediatric beds located elsewhere and five to ten beds on other nursing floors. Patients on other services often occupy five to ten designated orthopedic beds.

The attending staff is made up of 17 orthopedic surgeons, most of whom have at least one operative case each week. The resident staff, for the period under study, comprised four men. One resident served for the entire year, one for four months, and two for six months. In addition, three interns were on the service at various times for a period of one month each.

The nursing staff consists of a nucleus of 11 relatively permanent nurses, supplemented by four to six additional personnel at any given time. The orderlies, aides, and housekeepers comprise an additional 10 to 12 persons directly concerned with patient care.

Because of the nature of our infections, ward care was less suspect than the operating suite. The suite consists of five general rooms, a cystoscopy room, and a recovery room. Othopedic operations are done in all five rooms, interposed between other types of surgery, occasionally including septic cases. Six to seven hundred procedures are done in this suite each month.

In 1958 the orthopedic surgical service had 1,807 admissions. Eight hundred forty major operations and 144 open minor procedures were performed. Among this total of 984 cases there were 29 postoperative wound infections, for an over-all frequency of 2.95 per cent. Nineteen of these 29 infections, or about two-thirds, were superficial, in that they did not endanger the end result of the case. Ten infections, or about one-third, were deep, and materially affected the end result. In the latter group there were three deaths. One was due to a fulminating staphylococcus septicemia, one to pulmonary embolism, and one to a slow process of generalized debilitation developing over a 10-month course of osteomyelitis. Several of the minor infections recorded were quite superficial and might not have been considered significant except for the over-all increase in postoperative infections.

Factors Investigated

Organism

In 28 of the 29 infections, the organism cultured was a hemolytic staphylococcus, coagulase positive. Phage-typing was not

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Table 1

Effect of Prophylactic Antibiotics

Prophylactic Antibiotic Used*	
Deep infections	5
Superficial infections	9
Incubation period	10 days
Prophylactic Antibiotic Not Used	
Deep infections	5
Superficial infections	10
Incubation period**	8 days

* Conbiotic 3 cases
Chloromycetin 8
Erythromycin 2
Depocerocillan 1
Terramycin 1
Achromycin 1

** Excluded from this group is a case with an incubation period of three months.

done. Disk-type antibiotic sensitivity studies were carried out in each case, with variable and often misleading results. Occasionally the organism was reported sensitive to a drug which had been used prophylactically. Almost uniformly the organism was reported sensitive to chloramphenicol, and this was the drug most often used in treatment. In several instances the involved organism was reported sensitive to penicillin; however, treatment with this drug was attempted in only one case. Massive penicillin dosage in the range of 20 to 40 million units per day, as advocated by Petersdorf[2], is under consideration here at the present time, but was not tried in any of the cases reported here.

There was one infection in this series which was not staphylococcal, and it was due to a beta hemolytic streptococcus. The infection was of the spreading, subcutaneous type, with brawny overlying skin, and it was finally controlled after one month of intensive local and systemic treatment.

With the exception noted above, organisms other than staphylococcus were not encountered in our wound infections except as contaminants. During the period under study we did not notice any increase in the virulence of coliform or Pseudomonas organisms as reported by others[3].

Temporal variations

No relation was noted between the incidence of infection and the season of the year, nor any relation to changes in personnel. On July 1 two new residents and three new attending surgeons were added to the orthopedic staff. The operative load remained fairly uniform and did not coincide in any way with the random fluctuation of incidence.

Table 2

Summary of Wound Infections by Type of Procedure

Types	*No. Cases*	*No. Infections*	*Per Cent Infected*	*Deep Infections*	*Superficial Infections*
Hip Procedures	133	9	6.79	5	4
Femur procedures	63	4	6.34	2	2
Fusion or Laminectomy and fusion	76	7	9.21	2	5
Laminectomy alone	84	2	2.38	0	2
Total children	210	2	0.95	1	1
All other cases	418	5	1.19	2	3
Totals	984	29	2.95	12	17

Prophylactic antibiotics

Table 1 shows that in 14 of the 29 infections, a prophylactic antibiotic had been used postoperatively. In 15 cases no antibiotic was used. The relative incidence of superficial and deep infections was about equal. *It would seem that the use of prophylactic antibiotics did not alter the incidence of postoperative wound infections, nor did it affect the severity of those infections which developed.* The onset of symptoms in the untreated group occurred in eight days, as opposed to 10 days in the group which had received prophylactic antibiotics. One untreated case is omitted from the average because of an incubation period of three months, which was unique for both groups.

It is appreciated that in order to evaluate the efficacy of prophylactic antibiotics effectively, one would have to analyze all operations done on the service, with and without the use of antibiotics. In our opinion, however, these data suggest that prophylactic antibiotics are not beneficial in the average elective surgical procedure.

That the prophylactic use of antibiotics may be actively harmful has been repeatedly shown in other studies[4]. Altemeir and others[3], in the *Bulletin of The American College of Surgeons*, lists the improper use of antibiotics as a contributing cause of our present problem of drug-resistant bacterial infection.

Type of surgery

Table 2 illustrates the most important factor in this analysis. Three types of surgery—open femur procedures, open hip procedures, and lumbosacral fusions, accounting for about 27 per cent of the total operations performed — produced 68 per cent of the infections. The over-all infec-

tion rate was 2.95 per cent, while the infection rates for these three types of surgery were 6.34 per cent, 6.79 per cent, and 9.21 per cent respectively. The most interesting comparison is between lumbosacral fusion and lumbar laminectomy without fusion. In 76 fusions there were 7 postoperative wound infections, while in 84 laminectomies there were only 2 infections. Of these 2, one was a very minor "stitch" abscess and the other a deep infection following a particularly long and difficult dissection, in a back which had been operated on twice previously.

There were 2 infections in children, from a total of 210 pediatric cases. One of these was minor, the other deep and troublesome, though a good end-result was finally obtained. With few exceptions, operations in this group were done on extremities, using a pneumatic tourniquet.

A total of 6 infections followed the use of a pneumatic tourniquet. This represents a very small percentage in view of the large number of procedures done under tourniquet on our service. In 2 of the 6 cases, there was loss of tourniquet pressure during the procedure, with attendant soiling of the drapes and a bloody field.

The inference which we have drawn from the above cases is that uncontrolled oozing from raw bone, with associated hematomas, soiled drapes and soggy wound dressings, must have an extremely important bearing on the incidence and severity of postoperative wound infection.

Koch[5] has reported an incidence of 44 postoperative wound infections in 1,350 operative cases, for a total of 3.2 per cent. He, in turn, reported another published series with an infection rate of 9 per cent. In Koch's series, 38 of the 44 infections followed major operations lasting from two to five hours. This agrees with our finding that the more prolonged and difficult operations have the greatest propensity for infection.

Duration of surgery

It is known that the growth of an implanted colony of bacteria follows a definite pattern[6]. Initially there is a stationary phase, followed by a logarithmic increase in the number of organisms. A plateau is then reached, where the number of organisms being reproduced is equal to the number dying. In the final phase the death rate is accelerated as the colony exhausts its nutritive material. The relative duration of these phases of activity varies among species, staphylococci being relatively rapid growing organisms. The initial stationary phase is on the order of two to five hours. Thus it can be seen that even though the skin is adequately prepared, a long open operation provides ample time for airborne contamination, especially when one considers that the contaminating organisms may already have reached the phase of accelerated growth. With a generation time of 20 to 30 minutes, a small inoculation of organisms into devitalized tissue or clotting blood can progress to an important focus during a long case.

Table 3

Effect of Age

Severity of Infection	Average Age of Patient (Years)	Average Delay in Recovery* (Days)
Deep (12 cases)	52	34
Superficial (17 cases)	41	8

* 3 patients died under treatment

The average time required for operation in the cases of infection was more than one hour. In only one case was it less than one hour, and in many it exceeded two hours. The average was one hour and thirty-five minutes. This is greater than the time required for most procedures done on this service, and reflects the large number of open hip procedures and lumbosacral fusions, which require more time to perform well. It is logical that the longer a wound is exposed, the greater the risk of contamination.

Effect of age

The effect of age on the severity of infection is shown in table 3. It is not surprising that the elder and more debilitated patient is predisposed to deeper and more serious infections. Seven of the 12 deep infections in this series resulted from emergency procedures on the hip and femur in elderly patients.

Preoperative preparation of the skin

At the beginning of the period under consideration preparation of the skin was a matter of individual preference. Since then an effort has been made to adopt a standard procedure. It now begins with a shave on the day prior to surgery, followed by a 30-minute scrub with hexachlorophine soap (pHisoHex). The scrub is repeated on the

Table 4

Effect of Skin Preparations Used During the Last Six Months of 1958
Cases of Infection

Agent	No. Infections
pHisoHex	
1 application	2
2 applications	8
Ether, alcohol, merthiolate	0
Ether, iodine, alcohol	2

Random Sample of 134 Cases

Agent	No. Infections	Per Cent
pHisoHex		
1 application	14	10.4
2 applications	102	75.3
Ether, alcohol, merthiolate	3	2.3
Ether, iodine, alcohol	15	12.0

morning of the operation. In the operating room a final five-minute scrub with pHisoHex is followed by a rinse with aqueous zephirin. This regimen was in effect during the last six months of the period reported, and during that time there were eight infections where the complete preparation had been done.

Table 4 shows the distribution of preoperative skin preparations used during the last six months of 1958 on patients who acquired infections. pHisoHex, in two separate applications, was used in the preparation of 8 patients who later became infected. A single application of pHisoHex had been used in 2 patients, both emergency procedures, prepared entirely in the operating room. The remaining 2 were prepared with ether, iodine and alcohol.

These figures would seem to incriminate pHisoHex as a poor agent for skin disinfection; however, the large proportion of infections associated with pHisoHex in this series is due to its predominant use during the last six months of the year. To illustrate, a random selection of 134 operative cases from July and September shows that pHisoHex was used in the preparation of 87.5 per cent of the cases sampled.

Operating room personnel and equipment

Present at the time of surgery in the 29 cases of postoperative infections were 10 attending surgeons, 4 residents and 14 scrub nurses. Of the scrub nurses, no one was present at more than three of the operations which were followed by infections. Of the attending surgeons, two were present at four procedures and one at five. Among the remaining seven, each was present at from one to three operations on patients who became infected. Each of the residents is represented. In four of the cases of infection no resident was present at operation.

There is a considerable overlap of personnel in these cases, since a resident customarily scrubs in each case, and since several of the attending surgeons occasionally operate together. Because of this overlapping and the close communication among the staff, the ratio of infections to total procedures for each surgeon is considered artificial.

During the first six months of the year under study, 51 cultures were made from incisions, hands, and various static objects about the operating suite. Five cultures were made from surgeons' and nurses' hands following a prescribed scrub, of which three were positive for hemolytic staphylococci. None of the patients operated on after these scrubs became infected. Cultures taken from operative areas following preparation were negative in three of four instances; however, all were positive at the end of the procedures. Again, none of these wounds became infected.

Thirty-seven throat cultures were made among permanent operating room personnel. Of these, 16 were positive for hemolytic staphylococci, and another 17 grew streptococci or non-hemolytic staphylococci. This proportion of positive throat cultures (16 of 37) is somewhat higher than the nasopharyngeal carrier rate noted by Koch[5]. The carrier rate in his series ranged from 34 to 40 per cent; however, about one third of his carriers were fecal carriers only.

Among static objects about the operating suite, five out of six grew hemolytic staphylococci. The airborne spread of organisms was demonstrated by an agar plate exposed in the operating suite for one hour, which grew abundant colonies of hemolytic staphylococci.

Comment

The conclusion which we have drawn from this study is that the organism is ubiquitous in this hospital, and that the most important factor, barring gross contamination, is the susceptibility of the host. This susceptibility is apparently enhanced by bloody contused wounds, prolonged exposure, and soiled drapes.

Altemeir and others[3] discuss the emergence of drug-resistant strains of bacterial

organisms, which they attribute to the improper use of antibiotics and to violation of the basic techniques of asepsis and antisepsis, as a result of overreliance upon antibacterial agents. They present 10 recommendations for the control of drug-resistant wound infections, all of which deal with the intelligent use of antimicrobial drugs and extreme attention to proved aseptic and antiseptic techniques.

In the light of our findings, we would like to add to their recommendations the importance of maintaining as clean and dry an operative field as possible, realizing that there are many orthopedic procedures wherein raw bone is encountered and oozing is inevitable. We would also reiterate the basic surgical maxim of the most expeditious operative procedure commensurate with adequate exposure and closure.

Summary

1. Twenty-nine cases of postoperative wound infection are presented, with an analysis of individual pertinent factors.
2. The most important single factor to the majority of cases appears to be uncontrolled bleeding. Bloody contused wounds, soiled drapes, and soggy postoperative dressings appear to enhance the opportunity for wound infection. It is appreciated that in many orthopedic procedures, complete control of these factors is not always possible.
3. Advanced age and debility also appear to encourage infection, and to produce a more serious form of infection.
4. Prophylactic antibiotics seem to have served no useful purpose in this series. They have in fact worked to the detriment of the patient in some cases, by prolonging the incubation period.
5. Prolonged operating time was a generally consistent finding among the cases of infection.
6. Contamination by operating teams and equipment is the obvious source of infection, but considering the ubiquity of the organism in our study, host susceptibility is probably equally important in the development of the fully developed abscess.

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Respiratory Resuscitation

JOSEPH REDDING, M.D.

BALTIMORE, MARYLAND

Each year at least 50,000 people die in the United States as the result of accidents such as drowning, electric shock, drug poisoning, inhalation of carbon monoxide, chest injury, cardiac arrest, aspiration of foreign matter, and obstruction of the upper airway due to unconsciousness. During recent years much attention has been given to the resuscitation of patients suffering from cardiac arrest by immediate thoracotomy and manual compression of the heart. Since cardiac arrest, like the other accidents just mentioned, is due basically to inadequate oxygenation, immediate ventilation of the lungs for reoxygenation of the blood is essential in any attempt to reestablish circulation. If in the apparently dead person the heart is still beating feebly, respiratory resuscitation alone, without cardiac resuscitation, may restore an effective circulation. Cardiac resuscitation requires one rescuer to breathe for the patient and a physician to produce manual systole.

Read before the Second General Session, Medical Society of the State of North Carolina, Asheville, May 6, 1959.

From the Department of Anesthesia, Baltimore City Hospitals.

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*Hirsch, H. A., and Finland, M.: *New England J. Med.* 260:1099 (May 28) 1959.

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Establishment of an Open Airway

To ventilate the lungs and thus reoxygenate the blood, it is obviously necessary to have some route by which the resuscitative gas may enter the lungs. In most cases the natural air passage through the nose or mouth and pharynx is by far the most readily available and, because of lack of equipment, is the only route by which air or oxygen may be immediately introduced into the lungs of the patient. Occasionally the insertion of an endotracheal tube through the nose or mouth into the trachea will provide for better ventilation. In the great majority of cases, however, the necessary equipment for tracheal intubation will not be available or the rescuer will be unskilled in their use. Rarely, severe distortion of the face and neck due to trauma or disease will necessitate a third avenue of approach, namely, by tracheotomy. This procedure, however, is too time-consuming to permit the immediate ventilation that is vital to resuscitation. Furthermore, in the apneic patient, positive pressure inflation of the lungs through a tracheotomy is not easy to perform. Consequently we are in almost all situations limited by time and the immediate availability of equipment to using the natural air passage if we hope to accomplish a successful resuscitation.

The unconscious man is very likely to be asphyxiated from obstruction of the upper airway. Clinicians are very conscious of obstruction at the level of the lips, nose or larynx, and of obstruction by foreign matter such as vomitus. The most common type of obstruction frequently is overlooked—that is, obstruction of the oropharynx by the relaxed tongue, which is pushed against the posterior pharyngeal wall when the neck is flexed. This type of obstruction in the anesthetized patient was recognized more than 80 years ago by Esmarch. Recently Safar and co-workers[1] at the Baltimore City Hospitals studied a series of 80 lightly anesthetized, spontaneously breathing patients, in the supine and prone positions. It was noted that in both positions the airway was completely obstructed in 100 per cent of the patients when the neck was flexed—that is, when the chin was near the chest. With extension at the atlanto-occipital joint (namely, with the head tilted back as far as possible), 49 per cent had an open airway. With the head in extension, and with forward displacement of the mandible, the airway was completely obstructed in only 1 per cent. When the neck was flexed, an artificial oropharyngeal airway did *not* provide patency of the airway. When an artificial oropharyngeal airway was in place, with the head held in extension, none was completely obstructed. Contrary to common belief, the incidence and degree of obstruction was as great in the prone as in the supine position, with comparable degrees of flexion of the neck. In the prone position, the face was not easily accessible for manipulation of the head and jaw or for observation.

Ventilation of the Lungs

In the comatose patient who is not breathing spontaneously or is making very weak respiratory movements, it is necessary to find some means of moving air or oxygen into the lungs. One of two basic principles may be utilized to accomplish this purpose. Alternating compression and expansion of the thorax may be utilized to create the negative pressure within the air passage of the patient which will draw in the air. This is the basis for the use of the familiar tank respirator, which alternates the pressure surrounding the patient's chest, in turn expanding and compressing the thorax. The same principle was applied in the various manual or push-pull methods of artificial respiration so widely taught and practiced during recent years. Manual compression of the chest wall forced air from the lungs, while in theory elastic recoil of the thorax then drew air into the lungs.

The second principle utilized in ventilating the apneic patient is inflation of the lungs with positive pressure to the upper airway, followed by passive expiration[2]. This method of intermittent positive pressure breathing (IPPB) has long been used in anesthesia and in resuscitation in hospitals. It is ordinarily considered to be a method which may be used only with an oxygen source and certain types of breathing apparatus such as a bag-mask unit. It may be performed also, however, with atmospheric air—for instance, with the Kreiselman bellows or Ruben bag-mask unit or with exhaled air by mouth-to-mouth, mouth-to-airway, mouth-to-nose, mouth-to-mask, mouth-to-tracheal tube, or mouth-to-tracheotomy tube.

In a situation in which seconds make the difference between success and failure in resuscitation, the method for immediate application must not depend upon the presence or absence of any piece of equipment. Even when an oxygen source and equipment are near by, waiting a minute or two for them to be brought to the bedside may spell the difference between life and death.

Manual methods

The manual methods such as the Holger Nielsen (back-pressure armlift) do not rely upon any equipment for immediate performance. These and other methods of artificial respiration were studied at the Baltimore City Hospitals in a total of 49 experiments on 31 curarized volunteers and patients both with and without the use of an endotracheal tube. It soon became evident that obstruction of the upper airway was not taken into consideration when these methods were recommended. Without an endotracheal tube, trained operators were unable, in these experiments, to move more than dead space air in two thirds of the subjects studied, because of airway obstruction[3].

With an endotracheal tube in place a second reason for failure of the manual methods was noted[3]. These methods provide inadequate force for the movement of air in the presence of decreased lung thorax compliance. Compliance and airway resistance varied tremendously from patient to patient and under various conditions. Very little air could be moved in the obese patient or in those with chest or lung disease, even with an endotracheal tube in place. An effective method, therefore, must enable the operator to adjust the inflation pressure to the resistances encountered, and to see and feel immediately success or failure of each inflation effort.

Mouth-to-mouth methods

Elam and associates[4] and Greene and associates[4] showed in their studies with mouth-to-mask and mouth-to-tracheal tube breathing that inflation of the apneic patient's lungs with the operator's exhaled air can maintain normal oxygen saturation and carbon dioxide tension in the subject if the tidal volumes are increased above normal. A partially asphyxiated apneic subject can be reoxygenated with approximately five deep mouth-to-mouth inflations, and the oxygen saturation and end-expiratory carbon dioxide tension of the subject can be maintained at control levels almost indefinitely.

Evaluation of IPPB at Baltimore City Hospitals[5]

A technique which will permit a high degree of successful resuscitation must be one which can be applied also by laymen immediately in the absence of any equipment whatever. We have attempted to evaluate a number of IPPB methods at the Baltimore City Hospitals. A total of 250 rescuers previously untrained in IPPB performed various types of resuscitation on curarized adult volunteers who were lying supine on the floor. A volumetrically calibrated pneumograph was used to record continuously tidal exchange of the volunteer's lungs. The rescuer started one yard away from the victim's head. Elapsed time from the "go ahead sign" until the first inflation over 500 ml. was noted. The rescuer was recorded as successful with 500 ml. inflations if he produced 2 or more tidal volumes, each in excess of 500 ml. within 60 seconds.

Within two hours following a single demonstration which emphasized tilting back of the head, forward displacement of the mandible, tight-lip seal, and forceful blowing, 168 rescuers performed mouth-to-mouth breathing with the thumb-jaw-life technique[2]—that is, by supporting the mandible with the rescuer's thumb between the victim's teeth. Ninety-four per cent of them were successful.

Similarly, after one demonstration 97 rescuers performed the two-hands jaw-lift method of mouth-to-mouth insufflation[2]—that is, with both hands of the rescuer supporting the angles of the subject's jaw and both of the rescuer's thumbs retracting the lower lip. Eighty-eight per cent of them performed successfully.

After a single demonstration 88 rescuers performed mouth-to-airway breathing[2]. All of them inserted the airway successfully in 5 to 40 seconds, with an average insertion time of 12 seconds. Ninety-seven per cent of them were successful.

Thirty-five of these rescuers were called back to Baltimore City Hospitals one year following their initial performance. They were told that they were to attend a lecture on first aid, and were unaware that their ability to perform mouth-to-mouth breathing would be tested. They were called one at a time into a room where a

curarized subject was lying on the floor and were asked immediately to breathe for him. With the mouth-to-mouth method 83 per cent were successful, and by means of mouth-to-airway breathing 94 per cent were successful.

To evaluate difficulty in opening the mouth, two volunteers were anesthetized with scopolamine, meperidine and hyperventilation, and were rendered apneic without the use of curare drugs. Following a single demonstration 12 rescuers, performing in a statistically randomized sequence, ventilated the stiff volunteer with both mouth-to-mouth and mouth-to-nose breathing. With the mouth-to-mouth method 100 per cent were successful, while with the mouth-to-nose method 83 per cent were successful. In the 10 successful performances with the mouth-to-nose method, it was noted that the mouth had to be opened for expiration because of expiratory nasal obstruction.

Eighteen rescuers performed mouth-to-airway and mouth-to-mask breathing in a randomized sequence. Mouth-to-mask utilizes the nasal air passage, when no artificial oropharyngeal airway is used. With the mouth-to-airway technique all rescuers successfully inserted the mouth-to-mouth airway and produced tidal volumes in excess of 500 ml., while with mouth-to-mask breathing only 61 per cent of the rescuers were successful. The failures with mouth-to-nose and mouth-to-mask breathing were noted to be due chiefly to a higher incidence of partial expiratory obstruction, resulting in an increase of resting lung volume. Failures with mouth-to-mask breathing were also due to leakage between the face and the mask.

Conclusion

From these results it would appear that exhaled air resuscitation with mouth-to-mouth or mouth-to-airway intermittent positive pressure breathing provides an excellent resuscitative technique in the hands of physicians and laymen. The resuscitation technique for emergency use must be one which can be immediately applied in the absence of any equipment. If any adjunct is to be used, it must be extremely simple in construction and small enough to be portable and very widely available. The maneuvers necessary to maintain a patent airway—that is, head tilted back, mandible supported, a tight seal, and forceful blowing—must be stressed with *any* method.

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In 1940, Children's Hospital in Boston reported 305 cases of mastoid abscess. For most of these stricken youngsters, little more than palliative treatment could be administered to ease the agony while they were waiting for a difficult and painful operation which cost up to $1,000, and often meant partial loss of hearing. Today, many younger doctors have never seen a mastoid abscess. The "expensive" antibiotics permit physicians to control the infection for a cost of $15 to $20, and eliminate the need for surgery.—Mashberg, A.: Conquest at Bargain Prices, Memphis M. J. 34:263 (July) 1959.

The Problem of Narcotics As It Applies To Medical Practice

OKLA W. JOHNSON

GREENSBORO

The problem of narcotics has tormented the human race as far back as written records exist. Some 5,000 years before the birth of Christ the people in what is now Iraq recorded the earliest known information about narcotics. The great physician, Hippocrates, in the fourth century B.C., recommended white poppy juice for a variety of illnesses.

Opium is derived from the Greek word *opion*, meaning "juice." The Sumerians and Asyrians called it "joy juice," a term which leads us to believe that the addictive properties of the drug were known even in those far away times. Europeans used opium freely for the relief of pain as early as the sixteenth century. Its euphoric effect caused it to be regarded as a cure-all, and many people became addicted.

English traders picked up the practice of smoking opium in Calcutta in 1773, and Dutch traders adopted the habit in Formosa as prophylaxis against malaria. The English foisted the opium habit on the Chinese people and paved the way for the so-called Opium Wars, or the One Hundred Twenty-Five Years War. Chinese workers, brought into this country by the thousands, introduced opium smoking to the United States. The first American known to smoke opium was a man named Clendening, in 1868.

The discovery of morphine in 1803 and of the hypodermic needle in 1845 led to widespread addiction. Heroin — discovered in Dresden Germany, in 1898—was widely acclaimed as a panacea. Easy access and liberal use for medical indications caused thousands to become innocent victims of this drug.

The overproduction and unlimited sale of narcotics was allowed to continue for centuries, at the expense of untold social and economic distress. The medical profession and various molders of public opinion had become apprehensive concerning the misuse of opiates by the early 1900's. It was known that addiction had spread and was increasing among adults, especially women. Moreover, there was a sharp rise in the number of teen-age addicts to heroin.

Read before the Tenth District Medical Society, Asheville, October 14, 1959.

From the Bureau of Narcotics, U. S. Treasury, Greensboro.

Laws Restricting the Sale of Narcotics

Actually, our narcotic laws have been in effect only a long generation—forty or fifty years. Passage of the Federal Pure Food and Drug Act in 1906 did much to curtail the free use and easy distribution of narcotic drugs in patent medicines. Public alarm over the growing menace of addiction led to passage of the Harrison Narcotics Act in 1914. With only a few modifications, it is the law of the land today.

It has been conservatively estimated that prior to passage of these laws there were 200,000 addicts in the United States. Today the figure is placed at 60,000—46,266 cases having been actually reported as of December 31, 1958. Forty-five per cent of these cases were reported from New York, 14 per cent from Illinois, and 13 per cent from California. Other states accounted for 23 per cent. The racial distribution was as follows: Negroes, 59 per cent; Mexicans, 5.0 per cent; Puerto Ricans, 7 per cent; white, 27 per cent. Chinese and others made up the remaining 2 per cent.

Rising Incidence of Addiction in the Medical Professions

The United States

A shocking aspect of the narcotics problem is the rising incidence of addiction among medical men and in ancillary professions. The American Medical Association, recognizing the increase in addiction among the medical and para-medical professions, made a study of all patients admitted for addiction to meperidine (Demerol) to the United States Public Health Service Hospital at Lexington, Kentucky, from July 1, 1950, to September 30, 1953. One of the most disturbing findings of this study was that, of 457 persons addicted to Demerol, 186 were intimately associated with the medical profession.

The question was raised as to why doctors and nurses, with all types of narcotics available to them, should select a drug which is not preferred by the majority of addicts. A summary of responses to questioning is as follows:

1. All persons interviewed were vaguely aware of the addictive properties of Demerol but regarded it as less likely to produce toxic effects or addiction than other drugs. In the event of addiction, they believed that withdrawal of Demerol would be easier than withdrawal of opiates.
2. Demerol was more readily available than other narcotic drugs. Thefts from hospital and other stocks were more easily concealed because less care was taken to guard them.
3. Many felt that the stigma attached to the use of Demerol was much less than that associated with morphine or other potent derivatives of opium, and consequently less guilt was felt by the user.
4. Several addicts in the group professed to be "allergic" to the more common drugs and stated that they could tolerate only Demerol. Questioning revealed that "allergic" usually referred to unpleasant side effects such as nausea and vomiting, drowsiness, and, in a few instances, hives and other true manifestations of allergy.
5. Several felt that the observable signs of addiction to Demerol were less obvious to others than were the signs of addiction to opiates.

The data gathered in this study strongly indicated that the medical profession did not appreciate the addictive properties of Demerol, and that this lack of understanding had resulted in the high proportion of physicians, nurses, and members of allied professions who had become addicted to this drug. An insight into the increased consumption of Demerol may be gained from the following figures: In 1944, 3,563 ounces were used; in 1957, 376,284 ounces were used.

Great Britain and Germany

A report from Great Britain, submitted in July 3, 1958, states that medical and allied professions, comprising .75 per cent of the total population, contributes nearly 33 per cent of that nation's drug addiction. In the non-medical segment of the population, which does not have ready access to opiates, the incidence is 0.046 per 10,000, while in the medical professions it is 2.6 per 10,000. "It is inconceivable," the report states, "that the people — doctors, nurses, members of hospital staffs, etc.—who must be presumed to have knowledge of the addictive qualities of opiates, have the highest 'group addiction rate of the entire nation.' "

I hasten to point out that records on addicts and addiction in Great Britain are less accurate and complete than those of the United States and Canada. For example, in the trial of Dr. John Bodkin Adams, formerly an English physician, it was brought out that he had created more addicts among his patients than the total number of persons reported to be addicts in the entire country.

A report to the United Nations of March, 1959, entitled "Drug Addiction in the Medical and Allied Professions in Germany" contains additional data of an alarming nature. Fourteen per cent of the total number of addicts were medical men, while 68 per cent were members of the medical and paramedical professions. The ratio of addicts to non-addicts in the population as a whole is about 1 per 10,000.

Application of the Law to Medical Practice

Enough has been said about the history and present problem of narcotic addiction. Let us now consider the narcotics law as it applies to medical practice. I hope to be able to clarify some of the points about which I receive the most inquiries.

Many people do not realize that our federal narcotics laws are enforced by prosecutions based on tax frauds. Under our constitutional government the federal government does not have, and cannot exert, police power in controlling the importation, manufacture, sale, purchase, or giving away of narcotic drugs. All control is gained through the power of Congress to levy taxes and enforce the payment thereof. The federal narcotics law imposes special taxes upon all persons engaging in activities involving opium, cocoa leaves, marijuana, and the synthetic drugs classified as opiates. Since most physicians are familiar with the permissive features of this arrangement, I will not dwell upon it.

You may ask why I speak of narcotic law enforcement to a medical group. The reasons are multiple, but the most important is that in your practice each of you will, in some way, come in contact with the narcotic addict seeking his supply of drugs, which if supplied except in accordance with the law will make you liable under the law.

I know of no better way of acquainting you with the provisions of the law than by giving you the interpretation of the courts, for a mere reading of the law itself, without study and the application of other portions of the law, is of small benefit.

Principal and accessory

The law holds: *"A person dealing in drugs is required to ascertain at his peril whether that which he sells comes within the statute."* In a case involving this provision it would not be necessary to allege that a defendant knew the character of the drug he sold.

The law declares further: *"Whoever directly commits any act constituting an offense defined in any law of the United States, or aids, abets, counsels, commands, induces or procures its commission is a principal."* The acts of the principal become the acts of the accessory, who may be charged as having done the act himself. He may be indicted and punished accordingly, under the penal code making the accessory a principal.

Official order form

Turning now to the narcotics law and the way in which narcotic drugs may be sold legally, we find this quite definite statement, *"It shall be unlawful for any person to sell, barter, exchange or give away any narcotic drug except in pursuance of a written order of the person to whom such article is to be sold, bartered, exchanged or given, on a form issued in blank for that purpose by the Secretary of the Treasury."* The manufacturer must use this order form in buying from the importer, the wholesaler from the manufacturer, the pharmacist from the wholesaler, and the hospital from the wholesaler. All must use the order form in the business of selling, bartering, exchanging, or giving away narcotic drugs.

Prescription of narcotics

Let us now turn to the purpose of the prescription. A prescription, in order to legalize the possession of unstamped narcotic drugs and eliminate the necessity of using the order form, must be issued for legitimate medical purposes. The use of the prescription to distribute narcotic drugs is an exception to the law requiring all transfers to be by order form; but in order for the exception to be a statuatory exemption, it must comply with the provisions that the drug be furnished in good faith, to a bona fide patient, and in the course of professional practice. One court decision reads: "A physician prescribing narcotics for other than a bona fide patient and not in the course of professional treatment, is not protected by the statuatory exemptions." Another declares: "In order to be entitled to the benefit of the exceptions, the practice of the profession must be real and genuine, and the resort to it may not be had as a subterfuge to cover an otherwise unlawful dispensing of the taxable drug."

The responsibility for the proper prescription of narcotic drugs rests upon the practitioner, but a corresponding liability rests on the pharmacist who fills the prescription. An order purporting to be a prescription issued to an addict or habitual user of narcotics, not in the course of professional practice or treatment of disease, but for the purpose of providing the user with narcotics sufficient to keep him comfortable, by maintaining his customary dose, is not a prescription within the meaning and intent of the law, and the person selling such an order as well as the person issuing it may be charged with violating the law.

The court decision on this point is: "When a prescription appears with frequent regularity, that is sufficient to put the pharmacist on notice." Another states: "Knowledge by a pharmacist that a prescription was issued to gratify the holder's appetite, and not to cure disease or alleviate suffering, is essential to guilt, and negligent failure to inquire will not take the place of knowledge."

It is apparent that when a physician issues a prescription to be filled and charged for by a pharmacist, he does not personally sell or dispense the drug. The theory upon which he may be convicted is that he aided and abetted the druggist and thus became a principal.

It is impossible to make an inflexible rule which will cover all cases, and the

Bureau of Narcotics is not charged with the duty of laying down a fixed rule with regard to the use of drugs or the frequency of prescriptions. Congress has placed the responsibility for the proper prescription of narcotic drugs upon the physician, and he must exercise it *in good faith*. Congress has also placed a corresponding responsibility upon the pharmacist who fills the prescriptions to determine, *in good faith*, that the prescription was issued to a bona fide patient, for medical purposes only, and not for the gratification of addiction.

As you have noted, there has been no quotation of the law, either state or federal, which requires a pharmacist to fill a narcotic prescription and thereby accept the responsibility just outlined. Responsibility begins with the acceptance of the prescription and upon repetition assumes greater weight.

Legitimate Use of Narcotics

Most of this discussion has been focused on the dispensing of narcotics for drug addiction. I should like to point out, however, that there is no federal or state law designed to prevent the administration of such drugs to patients with incurable, painful, or fatal diseases. In cases of advanced carcinoma, tuberculosis, or in other chronic or perhaps acute disease, the physician is properly concerned primarily with relieving suffering and only secondarily with the problem of addiction. Proper and ethical medical practice, however, demands that certain principles be followed. Physicians prescribing narcotics for such patients should personally be in attendance. The diagnosis of a painful or incurable disease should be confirmed by consultation with another physician. All means of relieving pain other than by narcotics should be exhausted. When the administration of narcotics does become necessary, the physician should use less potent drugs first, and progress toward the potent drugs gradually. Precautions should be taken to insure that the amounts prescribed are no greater than those actually required for the particular patient, in order to avoid a surplus for diversion to illicit use.

Summary

1 The problem of narcotic drugs goes back to the beginning of recorded history.

2. The use of narcotics for relief of pain was common in Europe as early as the sixteenth century. The practice of smoking opium was picked up in Calcutta and spread throughout the world by commercial traders and immigrants.

3. The growing problem of drug addiction, accelerated by the discovery of morphine and the invention of the hypodermic syringe and needle, led to the passage of laws designed to regulate the distribution of narcotic drugs.

4. An alarming aspect of the narcotics problem is the disproportionately high incidence of addiction in the medical and paramedical professions.

5. Under state and federal laws the physician shares with the pharmacist the responsibility for dispensing narcotic drugs for bona fide medical reasons only.

* * *

NARCOTIC "DON'TS" FOR THE PHYSICIAN

(Prepared by the U. S. Bureau of Narcotics, Treasury Department)

Don't leave prescription pads around.
Addicts want them for effecting narcotic forgeries.

Don't write a narcotic prescription in lead pencil.
Avoid writing any Rx in pencil; many are changed to call for morphine.

Don't write for narcotics this way:
Morphine Ht ½ # x or
Morphine Ht ¼ # 10
Several X's or zeros can be added to raise the amount. Use brackets or spelling.

Don't carry a large stock of narcotics in your bag.
Addicts are on the lookout for these in doctor's offices and cars.

Don't store your office supply where patients can get at it.
Avoid storage near sink or urinal. The patient may ask to use these.

Don't fall for a good story from a stranger claiming an ailment that usually requires morphine.
The addict can produce bloddy sputum, simulate bad coughs or other symptoms. Make your own diagnosis.

Don't give a narcotic Rx to another without seeing the patient.
Addicts have posed as nurses to get doctors to prescribe narcotics.

Don't write for large quantities of narcotics unless unavoidable.
Diversion to addicts is a profitable business, as $1 for ¼ grain M. S.

Don't prescribe narcotics on the story that another MD has been doing it.
Consult that physician or the hospital records whenever possible.

Don't leave Rxs signed in blank at the office for nurses to fill in.
Signed blanks are bad practice and many have been stolen by addicts.

Don't treat an ambulatory case of addiction. Addicts must be under proper control.
Addicts go to several MD's at a time. Notify this Bureau.

Don't dispense any narcotics without keeping a record of it.
Bedside and office administration are permitted without record.

Don't buy your office narcotic needs on Rx blank in name of a patient.
The law requires you to use an official order form.

Don't hesitate to call this Bureau to get or give information. It will be held strictly confidenial.

Don't resent a pharmacist's call for information about an Rx you may have written.
The pharmacist is held responsible for filling forgeries. Please cooperate.

"A HOSPITAL IN DUBLIN"*

Frank E. Barnes, M.D.

A trip to Europe is a chastening experience for one who has lived in the United States and is fully convinced that we have a corner on all "know how" in medicine.

It was my privilege to visit the Dublin Rotunda Hospital which had a particular interest for me ever since I was a first year medical student. One of our faculty, whose wife died of eclampsia, said he had worked on the cause and alleviation of eclampsia for twenty-five years and knew no more then than at the beginning of his study. The doctor was high in his praise of Dr. Strogoff, who was working at the Rotunda with a great deal of success in treating eclampsia.

The Rotunda is a weather-beaten stone structure occupying one entire block; inside there is no "spit and polish" but there is an air of "know how" born of years of experience. The hospital was originally dedicated to the "care of poor and suffering women of Dublin" and even today a major part of the hospital is ward care.

Three doctors guided me through the hospital. First, we saw the clinic where a center table serves connecting dressing rooms. Next we visited the delivery room and I came just too late for a delivery. The patient is delivered while lying on her left side; no stirrups—nurses hold the legs. The theory is there is less trauma and pain for the patient. Forceps are rarely used and anesthesia is 2 cc. of chloroform which saturates an open cone; this is followed with ether. The patient remains in the delivery room until fully conscious and then spends six hours in a recovery room before retiring to her room. All blood work and intravenous medication is done by one doctor, who is called the phlebotomist.

The care of the newborn is quite different from our care. The Rotunda keeps the infant in a wire basket suspended at the foot of the mother's bed. However, in Dublin there are three lying-in hospitals with different infant care. One is similar to ours; the third is infant in bed with the mother in which case the mother assumes full care. This is easier because in Ireland 65% of mothers nurse their babies. The statistics show that the "in bed" baby has the lowest morbidity; the "crib at foot of bed" is next and the nursery care is the highest.

The Irish hospitals have a surfeit of nurses because their government subsidizes the student nurse. There is no tuition and a small weekly pay is given. We might try the same in our country.

Forty percent of the babies born in Ireland are delivered at home. A resident has a geographical area for which he is responsible and a team of two student nurses. A midwife who can give anesthesia is on call 24 hours a day. I asked about morbidity and the senior nurse answered, "We rarely have any trouble; in fact, we deliver breeches in gravid II and I think our figures will compare favorably with any in the world. I was in New York and I know 80% of deliveries could be done by, as you say, cops."

The prenatal care is excellent. Any woman with the slightest deviation from normal in blood pressure, kidney function or blood findings or heart trouble is kept in a special prepartum ward—sometimes as long as seven months—and treated until her condition is normal or until delivery. Incomplete abortions with a dilated cervix are taken care of at home unless the need of transfusion sends them to the hospital.

The pediatric ward consisted of compartments, individually heated and ventilated, with a nurse responsible for no more than four children. The doctors said this was the finest service in the world and I was wont to agree.

I wonder if a visiting physician should wander into one of our metropolitan hospitals, would he be shown the same courtesy I enjoyed?

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*Reprinted from the Nassau Medical News, September, 1959.

North Carolina Medical Journal

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DECEMBER, 1959

"SPACE SHIPS AND HUMAN DESTINY"

Although millions of words have been written about the first contact made by man with the moon, it is hard to think of a wiser comment than the one in the *Saturday Review* for September 26, by Editor Norman Cousins. Since its language cannot be improved, it is quoted in part, with the permission of Dr. Cousins:

"When viewed from the earth, the moon was behind a cloud at the moment the man-made rocket landed. But it was actually man who was behind the cloud. For he had not demonstrated his fitness to exist on his own planet, with all its natural advantages, much less earn the right to roam the heavens.

"Everything had been in man's favor on earth. He had air enough for his lungs. He had water—a rarity in the universe. The earth itself yielded food. His planet, billions of years ago, had become located on an orbit that was ideally situated in relation to the sun. One per cent nearer to, or farther from, the sun and the temperature would have been too great for human life to sustain. As it was, the combination of air, water, sunlight, and food had made the earth congenial for human life.

"This was only the beginning of the bounty. The earth dweller was the beneficiary of incredible personal gifts. He had intelligence, enabling him to . . . build on his own experience and create an increasingly improved environment . . .

"But he also had some defects. First, a staggering distortion in his sense of values. He could be worried about the possibility that his moon-bound rocket might contain some earth micro-organisms, and thus possibly contaminate some of the moon flora. But he was doing precious little about the increasingly dangerous contamination of his own atmosphere — contamination from radioactive materials he had poured into the air, from man-caused gases and smoke. And at the precise moment when his knowledge could enrich human life beyond imagination, he was putting most of that knowledge into the devices for eliminating himself altogether from the earth. He had somehow persuaded himself that the means of burning off all life went by the name of security. He insisted on keeping small weapons out of the hands of individual citizens but was perfectly willing to entrust planet-shattering weapons to large aggregations of human beings, so long as they were called nations. The idea that a collection of humans could not operate their local society without also constructing the machinery of law to govern them—this idea was regarded as absolutely essential. But he gave little thought to the kind of machinery that was required to govern nations, which had almost unlimited killing power at their disposal. Anything the nation did as a nation was usually justified; the needs of the human commonwealth went unattended.

"As a result, it now remains to be seen whether the gifts outweigh the defects. It remains to be seen whether intelligence can be put to full use in safeguarding life on this planet, or whether man's propensity

for absolute nonsense will put him in a position of absolute danger . . . For there is far more thinking today on what is required to assure survival for a single man inside a space ship than on what is required to assure survival for the entire human species on earth.

"We can celebrate the first physical contact of the earth dwellers with a heavenly body other than their own. We can proclaim our liberation from gravitational force and exult over our capacity to go calling in the universe. These are thrilling developments; our reach is totally free of boundaries.

"In all the excitement, however, it might be a good idea to find one small spot for a moment of quiet reflection. For the question that counts is not where we are going in the universe but where we are going on earth. Perhaps we may be able to arrange for a moratorium on megatons, neutrons, reactors, warheads, and space sleds long enough to ponder the question of human destiny. It is demeaning and insulting to believe that the human mind can calculate but not reason, that it can devise but not appraise, that it can concoct but not comprehend. Beyond this philosophical and spiritual exercise there is also the need for the individual to convince himself that he is not a spectator but a prime mover, someone who has the right to connect himself to important events and the power to influence the big decisions."

* * *

DR. JULIAN A. MOORE

Dr. Julian A. Moore of Asheville died about 2 P.M. Saturday, November 7. No doubt the final summons came as he would have wished, while he was at work in his office. His death is a great loss to the North Carolina medical profession. Although he was born in Georgia, most of his life was lived in North Carolina. He was graduated from the Wilmington high school, then from the University of North Carolina (B.S., 1916) and from the University of Pennsylvania Medical School (M.D., 1918).

After completing his hospital training at the Pennsylvania Hospital in Philadelphia and Garfield Hospital in Washington, he did general practice in Wilmington for five years—excellent preparation for his surgical career, which began, after thorough graduate training, in 1930. He was certified by both the American Board of Surgery and the American Board of Thoracic Surgery. Until the very end he was in active practice. He was chief surgeon of the Western North Carolina Sanatorium at Black Mountain, senior consulting surgeon at the VA Hospital in Oteen, and consulting surgeon to a number of other hospitals in and around Asheville. In 1953 a wing of the Western North Carolina Sanatorium was named in his honor.

Dr. Moore was president of the Buncombe County Medical Society in 1946, and of the Tenth District Society in 1953. He was vice president of the State Medical Society in 1943. At the Asheville meeting last May he was given citations from President Eisenhower and from Governor Hodges for his contributions to the physically handicapped.

Julian Moore made many contributions to medical journals, and devised a number of surgical instruments. He was not only a brilliant surgeon, but a fine citizen. He will be sadly missed in our Society. To his wife, children, and grandchildren this JOURNAL extends, on behalf of his many friends, heartfelt sympathy—and also fecilitations on the memory of a full and complete life.

* * *

DR. HUBERT A. ROYSTER

North Carolina lost one of its most distinguished medical men when Dr. Hubert A. Royster died at his home in Raleigh on November 7—just 12 days before his eightieth birthday.

Dr. Royster was an honor student and athlete both at Wake Forest College (B.A. 1891) and at the University of Pennsylvania Medical School (M.D. 1894).

He was the first doctor in North Carolina to limit his work to surgery—in 1906. From 1902 to 1910 he was dean of the University of North Carolina School of Medicine in Raleigh, and was professor of surgery at the Wake Forest School of Medicine from 1932 until his retirement in 1939. He was chief of surgery at Rex Hospital and at St. Agnes Hospital. He was also emeritus professor of surgery at the University of North Carolina School of Medicine when he died.

Dr. Royster was president of the Medical Society of the State of North Carolina in 1922, and was one of the founding fellows

of the American College of Surgeons. For many years he was secretary of the Southern Surgical Association, and was its president in 1926.

Dr. Royster wrote many articles for medical journals, and three books: *Syllabus of Therapeutics* (1899), *Appendicitis* (1927), and *Medical Morals and Manners* (1937).

His love of literature made him a "natural" for membership on the Editorial Board of the NORTH CAROLINA MEDICAL JOURNAL, and he was quite active during its early days. He proposed the name of the JOURNAL and made many helpful suggestions.

His literary ability combined with his long connection with North Carolina Medicine made him also the logical chairman of the Historical Commission, recommended by President Vernon in 1944 and appointed by President Paul Whitaker. It is to be hoped that the wealth of material he collected in the course of his chairmanship may yet be made available for use by his successor.

Dr. Royster came from a medical family. His father was Dr. W. I. Royster, and both his sons are doctors: Dr. Hubert A. Royster, Jr., of Bryn Mawr, and Dr. Henry P. Royster, of Philadelphia. A nephew, Dr. Chauncey L. Royster, is an internist in Raleigh.

In 1949 Dr. Royster made his last appearance before the State Society, where he spoke on "A Century and a Half of Medicine in North Carolina." He was introduced by his former student and colleague, Dr. William MacNider. Dr. MacNider's closing sentences are an appropriate conclusion to this editorial:

"All possible honors of a local and of a general character in surgical circles within this country have come to Dr. Royster. They have come as a result of the goodness of his purpose and the thoroughness with which he accomplished his ideal."(1)

1. North Carolina Medical Journal 10:394 (Aug.) 1949.

* * *

BLUE SHIELD AND THE NEW CHALLENGE

The American doctor's eternal struggle to preserve his professional freedom is now being waged in a new arena. Ten years ago, the big question was whether medicine could develop a viable prepayment program by its own voluntary effort, aided by labor, management and local community leaders. The alternative then was the threat of compulsory health insurance, governmentally operated and controlled.

The product of our initiative—and of the people's tremendous response—is the vast Blue Shield-Blue Cross complex, supplemented by a tremendous expansion of the insurance industry's effort in this field.

Both the medically sponsored nonprofit plans and the commercial insurance programs are based upon the traditional pattern of free choice of physician, fee-for-service, and the private relationship of patient and doctor.

In some segments of our economy today, both labor and management are showing a lively interest in providing medical care through a "closed panel" program, in which free choice would be limited, fee-for-service would be replaced by salaries or capitation payments, and the direct personal responsibility of the physician would be subordinated by collective controls.

The American Medical Association has acknowledged the legitimacy of these alternative programs and the right of the patient to choose the pattern or plan through which he wishes to prepay his medical care. This is realism.

But it is also realistic for us physicians to realize that ultimately we can preserve our traditional pattern of medical service only if our patients find that it meets their vital needs better than any other program.

Our own Blue Shield Plans offer us the best—and only—instrument through which we can control the economy of medicine and determine the shape of medical practice in the future.

But Blue Shield is *only* an instrument. The understanding, vision and leadership required to perfect this instrument—so that it will serve satisfactorily the needs of our patients—must come from us, acting through our county, state and national medical societies.

BULLETIN BOARD

COMING MEETINGS

U.N.C. Postgraduate Medical Course — Rocky Mount and Roanoke Rapids, January 14—February 18, 1960.

Conference of North Carolina County Medical Society Officers and Committee Members—Carolina Hotel, January 30.

Watts Hospital Symposium—Durham, February 10-11, 1960.

Sixth Annual North Carolina Conference on Children with Special Needs: The "Gifted Child." —Duke University, Durham, February 25-26, 1960.

Medical Society of the State of North Carolina, Annual Meeting—Raleigh, May 8-11.

American College of Surgeons, Sectional Meeting—Louisville, Kentucky, January 21-23.

International Medical Assembly of Southwest Texas—San Antonio, January 25-27.

Mid-South Postgraduate Medical Assembly—Peabody Hotel, Memphis, Tennessee, February 9-12, 1960.

American Academy of Occupational Medicine—Williamsburg Inn, Williamsburg, Virginia, February 10-12, 1960.

New Orleans Graduate Medical Assembly—Roosevelt Hotel, New Orleans, Louisiana, March 7-10, 1960.

American Academy of General Practice, Twelfth Annual Scientific Assembly—Philadelphia, March 21-24, 1960.

Eleventh Annual Symposium on Recent Advances in the Study of Venereal Diseases—The Palmer House, Chicago, April 7-8, 1960.

NEW MEMBERS OF THE STATE SOCIETY

The following new member joined the Medical Society of the State of North Carolina during the month of November, 1959:

Dr. Thad Jones Barringer, 3550 Hamstead Circle, Durham, North Carolina.

MARKER COMMEMORATING ORGANIZATION OF STATE SOCIETY UNVEILED

Officials of the State Medical Society unveiled a historical marker on Capital Square commemorating the organization of the Medical Society of the State of North Carolina in the Capitol Building in 1849.

Participating in the brief unveiling ceremonies were Dr. John C. Reece of Morganton, President and Dr. John S. Rhodes of Raleigh, Secretary. Also participating in the unveiling were Mr. James T. Barnes, Executive Director of the State Medical Society and. Dr. Christopher C. Crittenden, Director of the State Department of Archives and History.

A Raleigh newspaper of the 1849 era, the **North Carolina Standard**, carried an announcement at that time that a number of physicians assembled in the city and proceeded to organize. Dr. Frederick J. Hill, of Brunswick County, was chosen President of the Convention. A later issue of the same newspaper named the officers which were elected for the ensuing year, with Dr. Edmund Strudwick of Hillsboro, president.

The General Assembly enacted a special Act in 1858 which provided that "the Society known as the North Carolina Medical Society is hereby incorporated under the title 'The Medical Society of the State of North Carolina' with the Society continuing under that name to the present time."

From its beginning with only a few members, as we reckon organizations today, the Society has grown to a membership of about 3,200 physicians almost all of whom are actively practicing.

The Headquarters Office of the State Medical Society is located in Raleigh and all activities of the Society are coordinated by the Executive Director through this central unit.

Wording of the marker unveiled today is as follows:

MEDICAL SOCIETY
OF NORTH CAROLINA
Successor to earlier
group founded in 1799.
Formed here in 1849.
Dr. Edmund Strudwick

NEWS NOTES FROM THE BOWMAN GRAY SCHOOL OF MEDICINE

Dr. Harold O. Goodman, assistant professor of medical genetics, has received approval for a senior research fellowship in biochemical genetics, effective January 1, 1960.

* * *

Dr. Harold D. Green, professor of physiology and pharmacology, was presented with a Distinguished Service to Research special award at the December 5 meeting of the Board of Directors of the American Heart Association. The special awards are a recently established policy of the A.H.A. and are presented to those individuals who have served on the Research Committee of the A.H.A. for five full terms.

* * *

Dr. Ozmer L. Henry, Jr., instructor in preventive medicine and associate in clinical internal medicine, has been appointed to a "jury" of the

American College Health Association to review surveys of the student health services in colleges throughout the country. The purpose of the surveys is to evaluate and make recommendations concerning the health services.

* * *

Dr. Norman M. Sulkin, chairman of the department of Anatomy, was appointed chairman of the Section on Biological Sciences of the Gerontological Society at the November meeting in Detroit, Michigan. He was also appointed as a senior member on the Governing Council, representing the Biological Section and the editorial board of the **Journal of Gerontology** and the **Gerontological Newsletter.**

* * *

The Health Research Facilities Branch of the U. S. Public Health Service, Washington, D. C., has awarded a supplemental grant of $196,713.00 to the School for construction of medical research facilities and equipment.

* * *

Dr. Samuel P. Asper, Jr., associate dean and associate professor of medicine, Johns Hopkins University School of Medicine, discussed the "Revised Hopkins Curriculum," at a meeting of the Bowman Gray Medical Society on November 23.

* * *

The Student Health Department of the Bowman Gray School of Medicine of Wake Forest College sponsored a medical symposium on high school competitive athletics and sports at the college on November 18. The panel was composed of the following physicians: Drs. Jack Crutchfield, Lucile Hutaff, Frank Forsyth, George Frankl, and Henry Miller. Drs. Ozmer L. Henry, Jr., and Harold M. Barrow were moderators. The success of the symposium was evidenced by the attendance of over 200 athletic coaches, players, physical education instructors and youth activity directors. Similar programs are planned for the future.

News Notes from the Duke University School of Medicine

Duke University medical scientist Joseph W. Beard will direct a symposium on "Phenomena of the Tumor Viruses" to be sponsored next spring by the U. S. Public Health Service.

Tentatively scheduled for March in New York City, the two-day meeting will bring together virus tumor researchers from throughout the United States and several foreign countries.

The symposium will be financed by a grant of $8,731 to Duke University from the National Institutes of Health of the Public Health Service. Dr. Beard is chairman of the Tumor Viruses Committee of the USPHS Virology and Rickettsiology Study Section. He will direct the symposium in this capacity.

Purpose of the meeting, Dr. Beard noted, is to provide for exchange of ideas between scientists concerned with viruses as a possible cause of cancer.

The program will be centered around 12 papers by researchers from scientific institutions in this country, England, Holland, and France. Some 200 invitations to attend the symposium will be issued to investigators in virus research and closely related fields.

Professor of surgery at Duke, Dr. Beard is director of the Medical Center's program of virus study in relation to cancer.

* * *

Doctors are made, not born, but the son of an M.D. probably has a better than average likelihood of following in father's footsteps.

This is borne out by enrollment statistics at the Duke University Medical School, where one of every six students is the son of a physician or dentist.

Numbering 53 in a total medical student body of 321, the M.D. candidates from doctors' and dentists' families represent 17 states, Washington, D.C., and Puerto Rico. Their fathers include general practitioners, surgeons, pediatricians, radiologists, internists, pathologists, and a medical missionary.

Duke Medical School Dean W. C. Davison does not believe that physicians' sons have the edge on anyone else when it comes to making a good doctor. Neither do they stand an unusually good chance of getting into medical school in the first place.

He explains the large proportion of doctors' sons at Duke by noting that more such persons apply for medical school.

North Carolina Heart Association

A limited number of Research Fellowships are being offered by the North Carolina Heart Association with a deadline for applications of January 15, 1960. The one-year grants carry a stipend of from $3,800 to $5,200, depending on the number of the applicant's dependents. Applicants must hold the degrees of Doctor of Medicine, Doctor of Philosophy, Doctor of Science, or an equivalent degree and may apply for support in the field of cardiovascular function and disease or of related fundamental problems.

The 1959 Fellowships went to Drs. Roberta O'Dell of Duke, William Wood of U.N.C. Medical School, and Richard Obenour of the Durham V. A. Hospital. The Fellowships may begin at any time between July 1 and October 1, 1960.

Application forms may be obtained from the North Carolina Heart Association, Miller Hall, Chapel Hill.

RANDOLPH COUNTY MEDICAL SOCIETY

The Randolph County Medical Society held its annual meeting November 23, in Asheboro. New officers for 1960 were elected and were: Dr. E. D. Shackelford, president; Dr. W. H. Fowle, III, vice president; and Luke Eller, secretary and treasurer. H. O. Burnette, M.D., the retiring president, presided at the meeting.

The new officers will be installed at the Christmas festivities, to be held at Asheboro Country Club, December 15.

AMERICAN RHINOLOGIC SOCIETY

The American Rhinologic Society has elected the following officers for 1959-1960:

President—Dr. Roland M. Loring, Chicago; president-elect—Dr. Ivan W. Philpott, Denver; vice president—Dr. Raymond L. Hilsinger, Cincinnati; secretary—Dr. Robert M. Hansen, Portland, Oregon; treasurer—Dr. George G. Fischer, Wilmette, Illinois; directors: Drs. Leland R. House, Los Angeles; Lewis E. Morrison, Indianapolis; and Amos E. Friend, Manchester, Connecticut.

* * *

A seminar in "Reconstructive Surgery of the Nasal Septum and External Nasal Pyramid" will be held in New Orleans, February 10-13, under the auspices of the Department of Otolaryngology (Dr. Val Fuchs, chairman), Louisiana State University Medical School, and the Charity Hospital, in cooperation with the American Rhinologic Society.

For further information, write to Dr. Robert M. Hansen, secretary of the American Rhinologic Society, 1735 North Wheeler Avenue, Portland 12, Oregon.

AMERICAN ACADEMY OF GENERAL PRACTICE

The American Academy of General Practice will hold its twelfth annual Scientific Assembly, March 21-24, 1960, in Philadelphia's Convention Hall. More than 4,000 family doctors and 3,000 residents, interns, exhibitors, and wives will attend the four-day program high-lighting recent progress in medicine and surgery.

The Philadelphia Assembly program lists 31 prominent medical educators who will discuss a variety of subjects ranging from arthritis and anemia to surgery, geriatrics, and mental health. The doctors will also visit more than 100 scientific and 300 technical exhibits. Many of the scientific exhibits will relate directly to the scientific program. They have been carefully selected to answer questions posed by the doctor in active practice.

During the meeting, the doctors will have a chance to be on the other end of a stethoscope during physical examination sessions. More than 600 doctors took physical examinations at the last Academy meeting. Many learned, for the first time, that they needed immediate medical attention.

The Academy Assembly is this year combined with the Philadelphia Postgraduate Institute.

UNIVERSITY OF OKLAHOMA MEDICAL CENTER

A program on adrenal steroids has been developed for the Third Annual Oklahoma Colloquy on Advances in Medicine to be held March 24-26 at the University of Oklahoma Medical Center, Oklahoma City.

Scientific papers will cover clinical application of the steroids in endocrinology, infectious diseases, gastroenterology, rheumatic disease, hematologic diseases (including the leukemias and immunohematologic disorders), neoplastic, collagen, renal, and allergic diseases.

Additional information may be obtained by writing the Office of Postgraduate Education, University of Oklahoma Medical Center, 801 NE 13, Oklahoma City, Oklahoma.

AMERICAN HOSPITAL ASSOCIATION

Legible footprinting of infants at birth is a positive means of identification vital in cases "where law enforcement has an interest", J. Edgar Hoover said in an article published recently.

Footprinting should not, he said, replace other methods of identifying infants, such as bracelets carrying the baby's name, but should rather supplement such devices.

He noted that just as on the hands, the arrangement of ridges on the soles of the feet is "never duplicated in other persons".

Footprinting is more practical than fingerprinting in infants, he said, because the area is larger and is also more rigid due to the lesser movement of the joints.

Hospital personnel need not be taught to read footprints, he said. He pointed out that this can be done by an expert. However, to insure legibility, Mr. Hoover believes there should be "a brief footprinting course . . . in all nurses' training schools". He said that "two- or three-hour courses by qualified fingerprint technicians should suffice."

WORLD MEDICAL ASSOCIATION

The German Medical Association, host of the XIVth General Assembly of The World Medical Association, scheduled to convene in West Berlin, September 15-21, 1960, is planning to have an extensive Medical Film Program.

All medical associations are cordially invited to present to the German Medical Association their recommendations as to outstanding postgraduate medical teaching films, particularly those produced in their country, which should be given consideration by the Special Committee that has been appointed to select the films to be shown.

The World Medical Association Headquarters Secretariat is issuing a special "Film Recommendation Sheet" for the use of the member associations.

INTERNATIONAL MEDICAL ASSEMBLY

The twenty-fourth annual session of the International Medical Assembly of Southwest Texas will be held in San Antonio, Texas, January 25-27, 1960 at the Hilton Hotel.

Those interested in receiving further information or in registering may write Dr. A. O. Severance, President, or Mr. S. E. Cockrell, Jr., Executive Secretary, 202 West French Place, San Antonio 12, Texas.

In Memoriam

Hubert Ashley Royster, M.D., Sc.D., F.A.C.S.
November 19, 1871—November 7, 1959

After several years of failing health, North Carolina's most outstanding surgeon quietly passed away. The son of Dr. W. I. and Mary (Finch) Royster, he graduated from Wake Forest College in 1891, and from the University of Pennsylvania Medical School in 1894. After a year as resident physician at The Mercy Hospital at Pittsburg, Pennsylvania, he returned to Raleigh and entered the practice of medicine with his father. However, his first interest was surgery, and in 1906 he became the first man of North Carolina to limit his practice solely to that of surgery. Ever the student, he made a record with the Board of Medical Examiners that is outstanding to date. As ever the teacher, he was dean and professor of gynecology at the University of North Carolina's Medical Department, which was in Raleigh from 1902 to 1910. Loyalty and respect for the dignity and integrity of his fellow physician made him take the position of professor of gynecology in deference to Dr. Agustus Knox, who was professor of surgery.

To list the honors bestowed upon him for his indefatigable efforts to ever raise the standards of the practice of medicine and surgery in his state and in the nation would need space to list all of the outstanding medical and surgical organizations in this country as well as intimate associations with the great men of surgery in our nation.

It suffices to say that for years he was a member of the editorial board of this JOURNAL; he served with distinction as secretary to the Board of Medical Examiners of North Carolina from 1914 to 1920, and President of the State Association in 1922.

At the insistence of Secretary of the Navy Daniels in World War I, he kept his active practice in Raleigh but made weekly trips to Washington as a medical member of the Advisory Committee of the Council of National Defense.

In 1901 he married the former Miss Louise Page of Maryland, and is survived by Dr. Hubert Ashley Royster, Jr., and Dr. Henry Page Royster, who carry on the Royster heritage in pediatrics and surgery; as well as a daughter, Mrs. Thomas Oxnard of Savannah, and eight grandchildren.

Forced to retire from the active practice of surgery in 1939 because of a heart attack, he continued his ever present interest in teaching and writing, insisting always that character and truth are the most important things in life and forever battling that the English language be spoken with accuracy.

In an editorial tribute by Jonathan Daniels, the very essence of this man was expressed: "He was a man sometimes outspoken in impatience with mediocrity. He had a ready scorn for men who did not maintain standards which he always honored in his profession and his life. He hated sloppy work and sloppy men, and his admiration for men of skill in his profession never surpassed his demand for character as a first essential in medical practice.

". . . Age took the scapel from his hand sometime ago. Now death has removed him as a man honored among us. Still in hope and in the science of healing in North Carolina his life remains as an example for the future and a part of the best heritage of our past."

Alexander Webb, Jr., M.D.

Donald Edward Robinson, M.D.
1901-1959

WHEREAS, our Creator, in His infinite wisdom, did give to this world, and particularly to the people of Alamance County and Burlington, N. C., a great and humble physician;

And, WHEREAS, our Maker, according to His will, yet not to our understanding, did see fit to remove from us our beloved colleague and friend, Dr. Donald E. Robinson;

And, WHEREAS, as an outstanding and devoted pediatrician, Dr. Donald E. Robinson did tirelessly and unselfishly minister to the needs of all children regardless of race, color, creed or financial status;

And, WHEREAS, as a community leader, Dr. Donald E. Robinson was instrumental in securing for Alamance County a full time Health Department, better library facilities, increased school supplements for a more enriched curriculum, and improved city government;

And, WHEREAS, through the interest of Dr. Donald E. Robinson the Alamance County Tuberculosis Sanatorium was given;

And, WHEREAS, as a Boy Scout leader in the Cherokee Council, Dr. Donald E. Robinson did render many years of service with emphasis on scout health and safety, and did give substantially of his finances for improved equipment and facilities for scouting;

And, WHEREAS, Dr. Donald E. Robinson also gave willingly of his time, talents and means in

suport of the Community Council, the United Fund, the City Recreation Department, the McDade Museum and the Community Y.M.C.A.;

And, WHEREAS, to his family, to the many children and parents to whom he rendered devoted service, and to our entire community, the loss of Dr. Donald E. Robinson has brought great sorrow;

And, WHEREAS, this community and this Medical Society will continue to miss the outstanding leadership and service of Dr. Donald E. Robinson;

Now, THEREFORE, be it RESOLVED that the Alamance-Caswell Medical Society hereby express its deepest appreciation and its profound sense of loss in the passing of Dr. Donald E. Robinson on July 19, 1959;

And be it further RESOLVED that a copy of this RESOLUTION be published in the **North Carolina Medical Journal** and a copy be placed in the minutes of the Alamance-Caswell Medical Society, and that a copy be sent to Mrs. Robinson and to his son and daughter.

Paul F. Maness, M.D.
John T. King, M.D.
Donald M. Ross, M.D.

BOOK REVIEW

Our Nuclear Adventure, Its Possibilities and Perils. By D. G. Arnott. New York: Philosophical Library, 1958.

This book is a timely and well written review of the problem of nuclear energy particularly from the aspects of its wartime and power use potential. The author does not attempt a significant review of the subject from the standpoint of the medical or biologic applications—although he discusses briefly some of the hazard potentials.

The style of writing and manner of presentation of the subject are lucid; and a seemingly difficult subject is presented so that anyone of average educational attainment may understand and read with keen pleasure.

There is first a presentation of basic information about atoms, radioactivity, and how radiation affects living things. A rather detailed description of nuclear explosions follows, with a considerable emphasis upon the "fall-out" problem.

An interesting exposition of thermonuclear power follows particularly as pertains to the program in Britain.

The author concludes with an expression from his deep sociopolitical conscience of the necessity for international control and of some of the absurdity of much of the "secrecy" which accompanies the advances made with atomic energy.

The Month in Washington

A special committee of consultants to the federal government has recommended what was termed an urgent, essential program designed to maintain the present ratio of physicians in a sharply expanding population.

Dr. Leroy E. Burney, Surgeon General of the Public Health Service, gave his personal approval to the recommendations made by his 22-member Consultant Group on Medical Education after about a year's study. But he said he couldn't indicate yet "the extent to which they can be incorporated" in next year's proposals of the Department of Health, Education and Welfare.

The Consultant Group recommended expansion of existing medical schools and construction of 20 to 24 new ones with federal help, federal scholarships for medical students, and greater efforts in the field by states, local communities, foundations, individuals, industry, and voluntary agencies.

The Group said that the present ratio of 133 doctors of medicine and 8 doctors of osteopathy per 100,000 population is "a minimum essential to protection of the health of the people of the United States."

To maintain this ratio, the Group said, "the number of physicians graduated annually by schools of medicine and osteopathy must be increased from the present 7,400 a year to some 11,000 by 1975—an increase of 3,600 graduated.

"To meet the country's need for physicians for medical care, teaching, research, and other essential purposes will require an immediate and strenuous program of action by the nation as a whole," the Group's 95-page report stated.

"This program must safeguard and improve the quality of medical education as well as bring about the need substantial increase in the number of physicians."

The no. 1 recommendation of the Group was for the federal government to appropriate over the next 10 years funds—estimated at about $500 million "on a matching basis to meet construction needs for medical education," including necessary teaching hospitals.

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The Month in Washington

(Continued from page 531)

"The Consultant Group is convinced that the nation's physician supply will continue to lag behind the needs created by increasing population unless the Federal government makes an emergency financing contribution on a matching basis toward the construction of medical school facilities," the report said.

The Group also said research grants to medical schools "should cover full indirect costs so that medical schools are properly reimbursed for the contribution of medical education to medical research."

These two recommendations were in line with American Medical Association positions on the matters.

The Group also urged "more generous public and private support for the basic operations of medical schools." Such support, the report added, "must come from many sources, including state and local appropriations, endowments, gifts and grants, universities, and reimbursement for patient care."

Most of the consultants were physicians or educators. They included Dr. Julian Price of Florence, South Carolina, a member of the A.M.A. Board of Trustees, and Dr. Edward L. Turner, Director of the A.M.A. Division of Scientific Activities.

Highlights of the Group's report included:

—To maintain the present physician-population ratio, the expected 1975 population of 235 million will require a total of 330,000 doctors of medicine and osteopathy.

—There also must be 12,000 entering students in 1971, as against about 7,600 a year now.

—"In a very real sense, the needs for physicians cannot be met by numbers alone. They will be met only as an expanded program maintains and enhances the quality of medical education."

—The entry of more physicians into research, industrial medicine and similar activities "has made possible much of the progress of modern medicine." But it also resulted in "relatively fewer physicians devoting full time to patient care."

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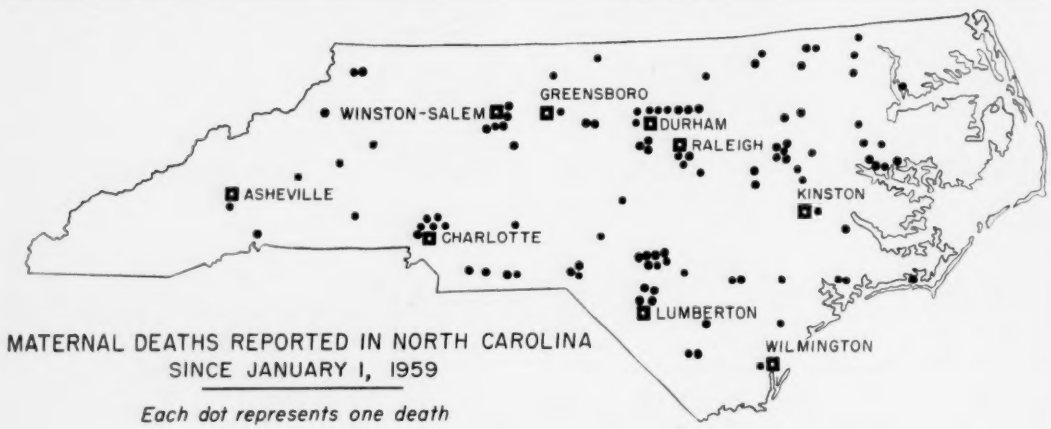

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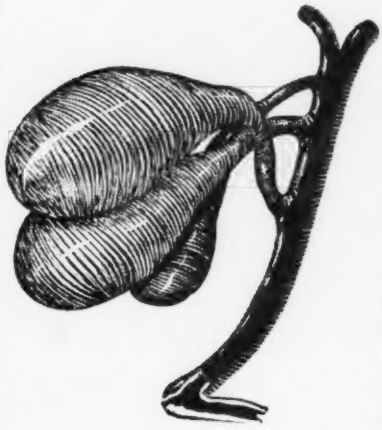

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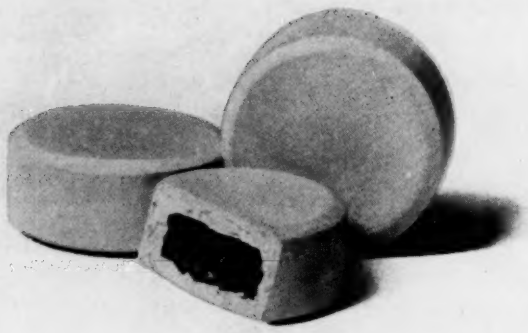

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*Thompson, R. E., and Hecht, R. A.: Am. J. Clin. Nutrition 7:311-317 (May-June) 1959.

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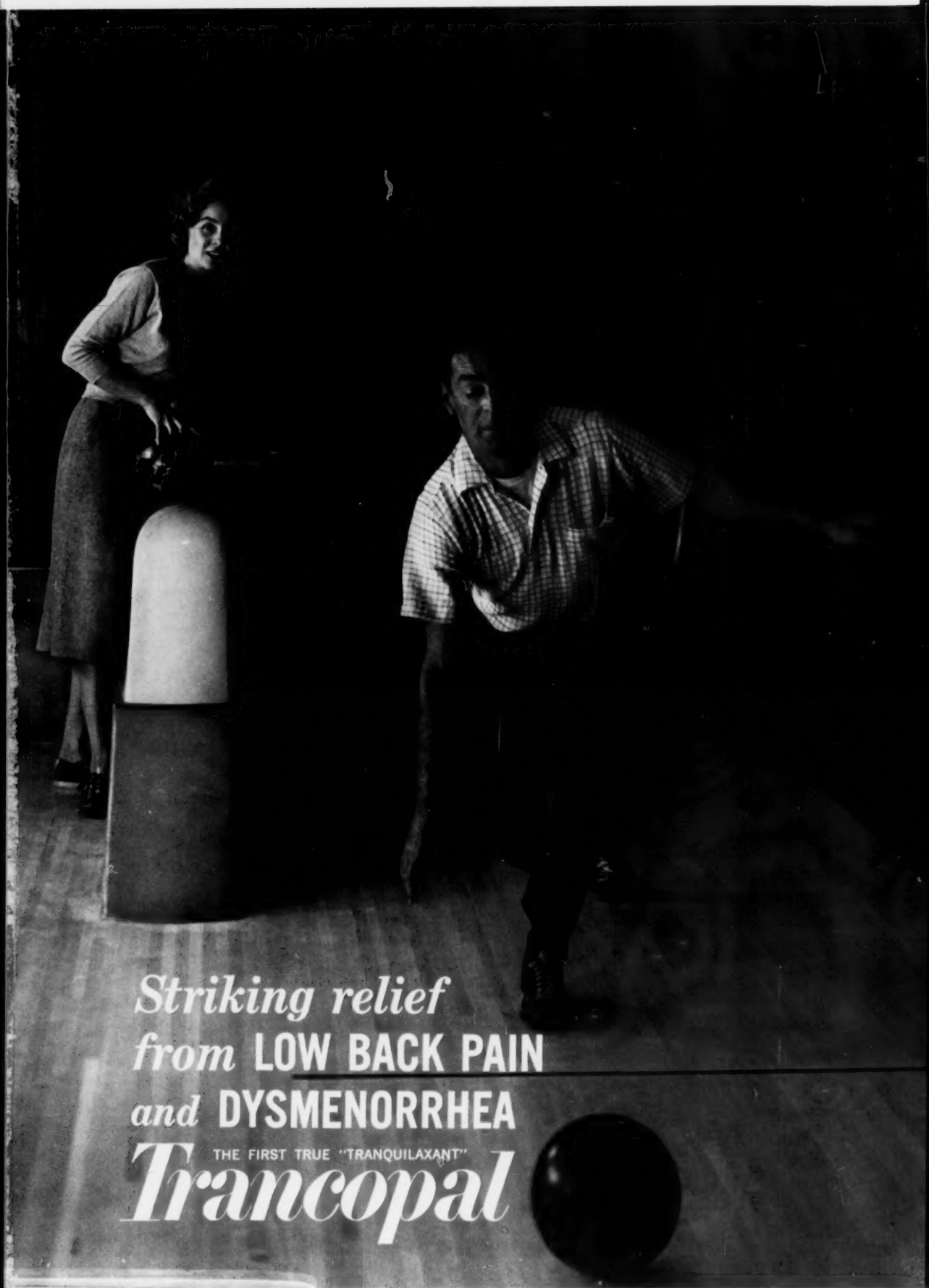
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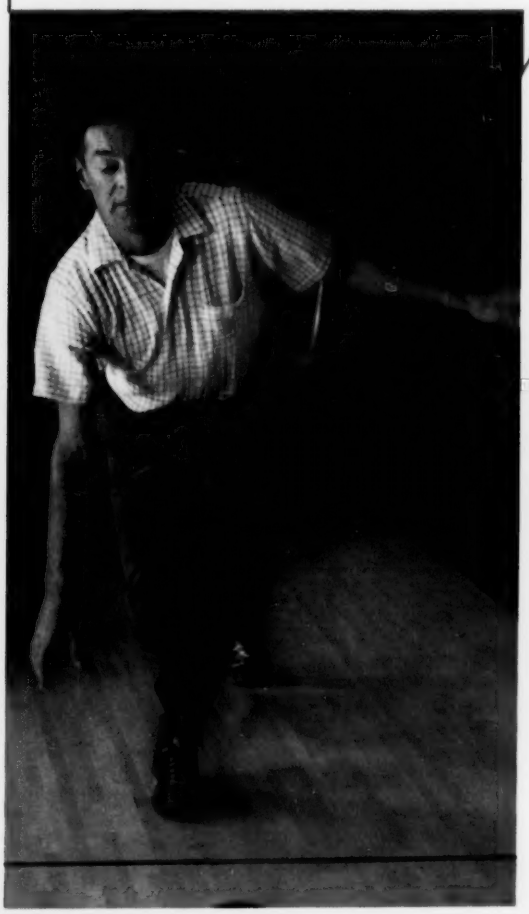

Case Profile*

A 42-year-old truck driver and mover injured his back while moving a piano. The pain radiated from the sacral region down to the region of the Achilles tendon on the right side. X-rays for ruptured disc revealed nothing pertinent. The day of the injury he was given Trancopal immediately after the physical examination. Although 100 to 200 mg. three times a day were prescribed, the patient on his own responsibility increased the dosage of Trancopal to 400 mg. three times a day. This dosage was continued for three days and then gradually reduced over a ten day period. During this time, the patient continued to drive his truck. The muscle spasm was completely controlled and no apparent side effects were noted.

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Indications [1-6]

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Osteoarthritis
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References: 1. Collective Study, Department of Medical Research, Winthrop Laboratories. 2. Lichtman, A. L.: New developments in muscle relaxant therapy, *Kentucky Acad. Gen. Pract. J.* 4:28, Oct., 1958. 3. Lichtman, A. L.: Relief of muscle spasm with a new central muscle relaxant, chlormezanone (Trancopal), Scientific Exhibit, Meeting of the International College of Surgeons, Miami Beach, Fla., Jan. 4-7, 1959. 4. Ganz, S. E.: Clinical evaluation of a new muscle relaxant (chlormethazanone), *J. Indiana M. A.* 52:1134, July, 1959. 5. Mullin, W. G., and Epifano, Leonard: Chlormezanone, a tranquilizing agent with potent skeletal muscle relaxant properties, *Am. Pract. Digest Treat.* 10:1743, Oct., 1959. 6. Shanaphy, J. F.: Chlormezanone (Trancopal) in the treatment of dysmenorrhea; a preliminary report, *Current Therap. Res.* 1:59, Oct., 1959.

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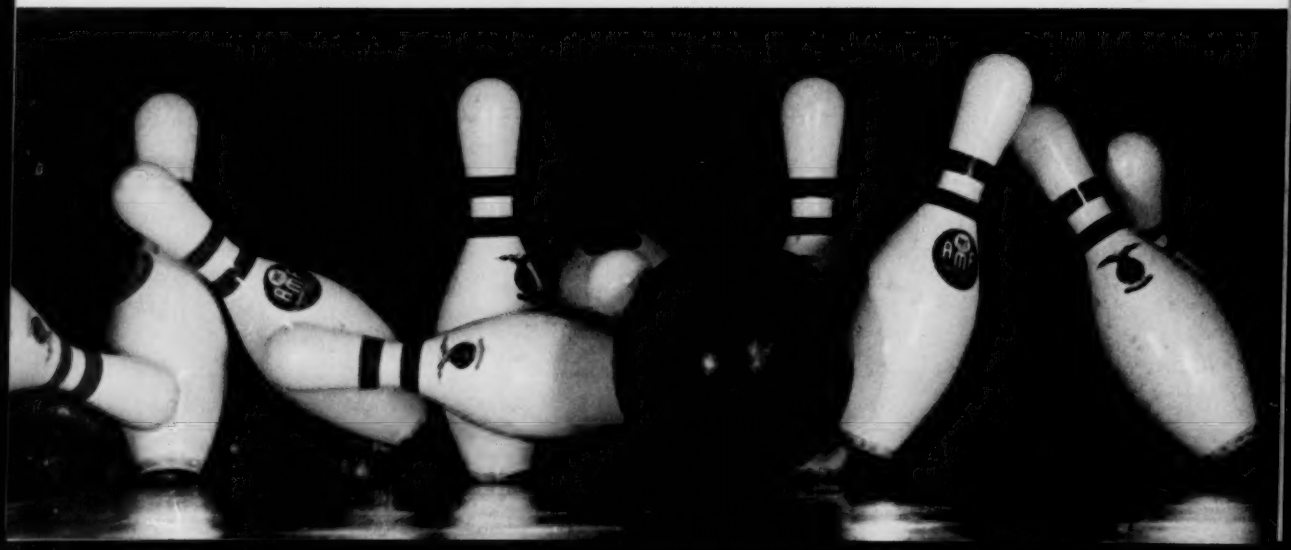

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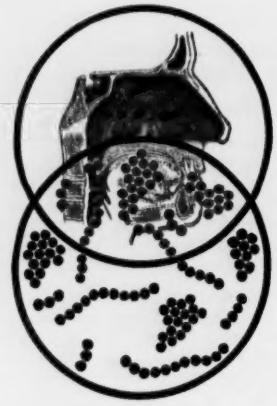

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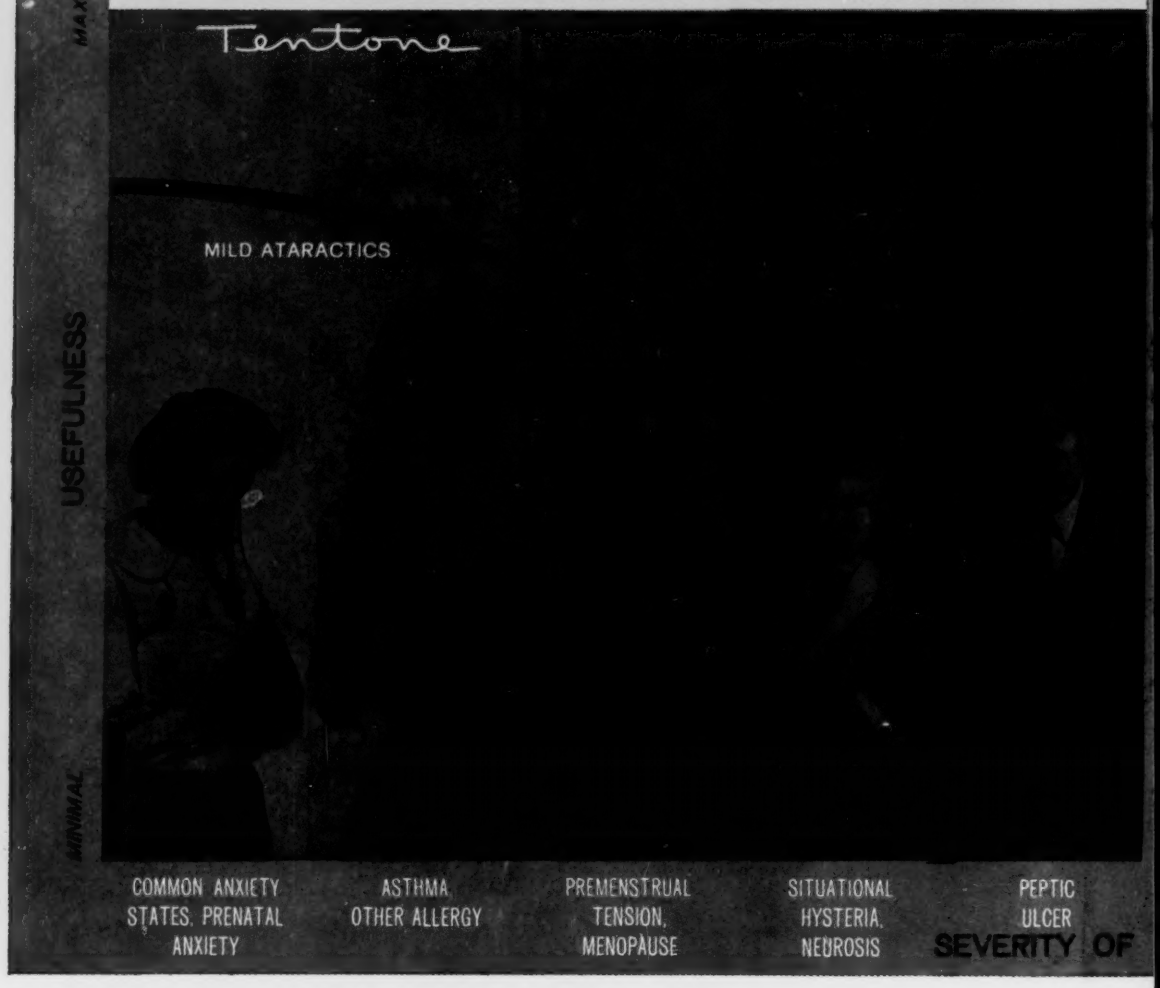

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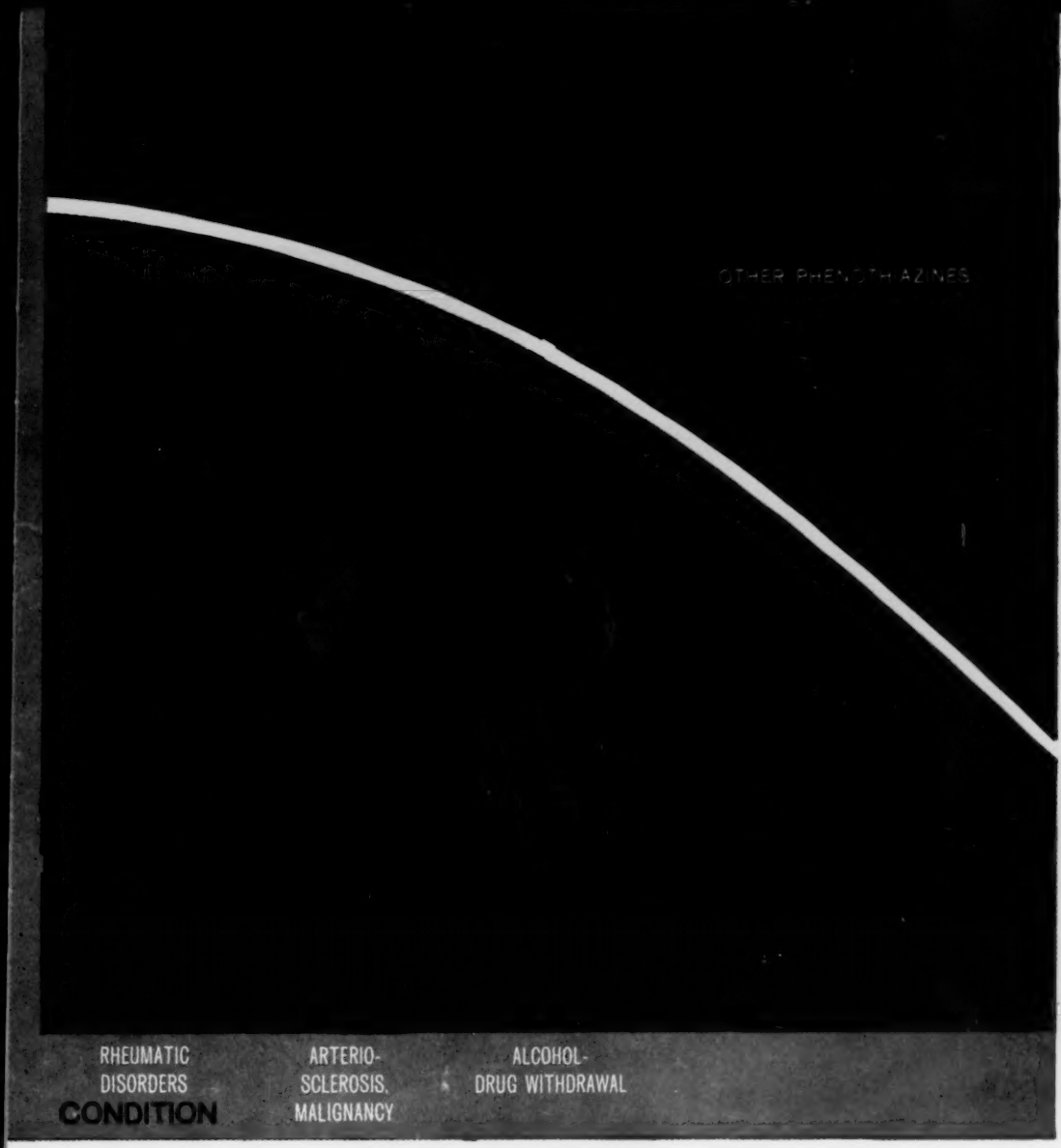

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1. Bodi, T., and Levy, H.: Clinical report, cited with permission. 2. Wetzler, R. A., and Phillips, R. M.: Clinical report, cited with permission. 3. Prigot, A.: Clinical report, cited with permission. 4. Gosline, E., *et al.*: *Am. J. Psychiat.* 115:939 (April) 1959. 5. Turvey, S. E. C.: Clinical report, cited with permission.

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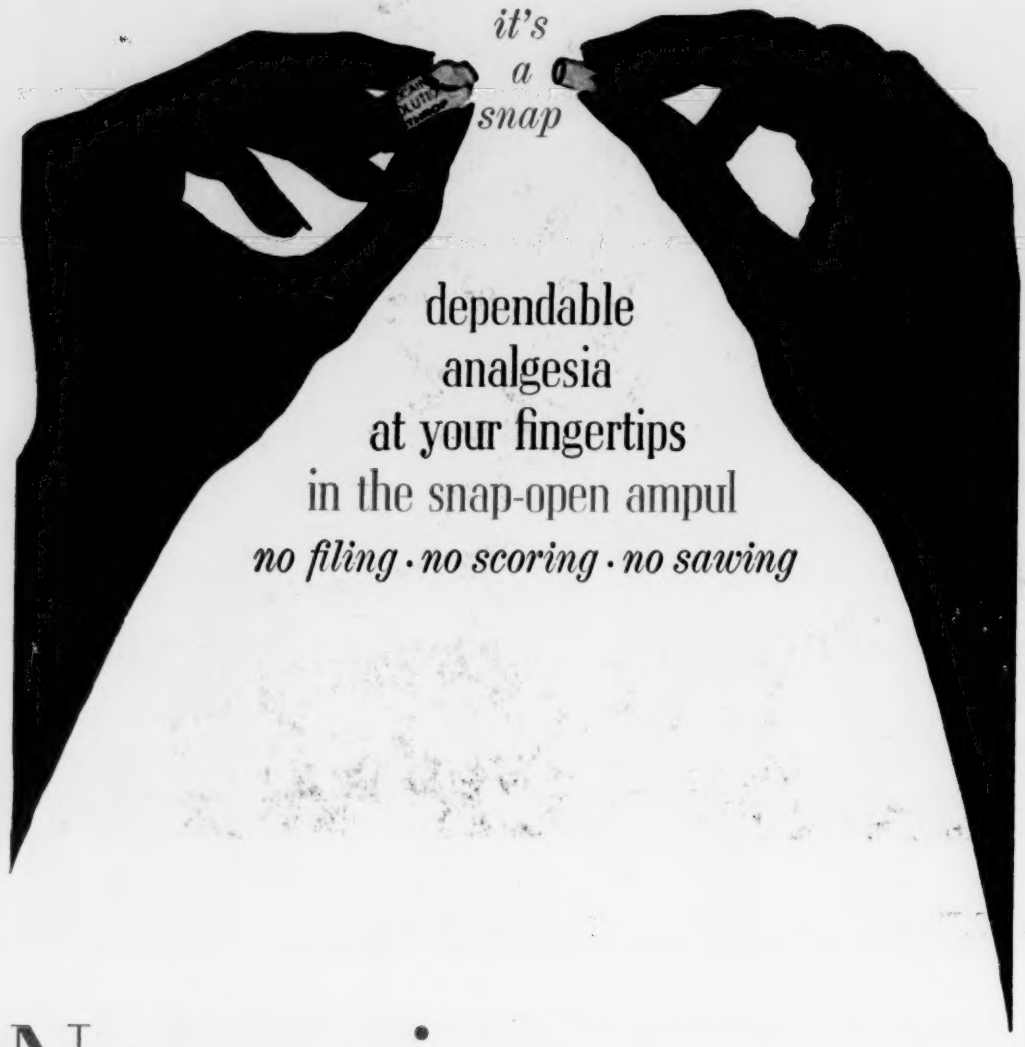

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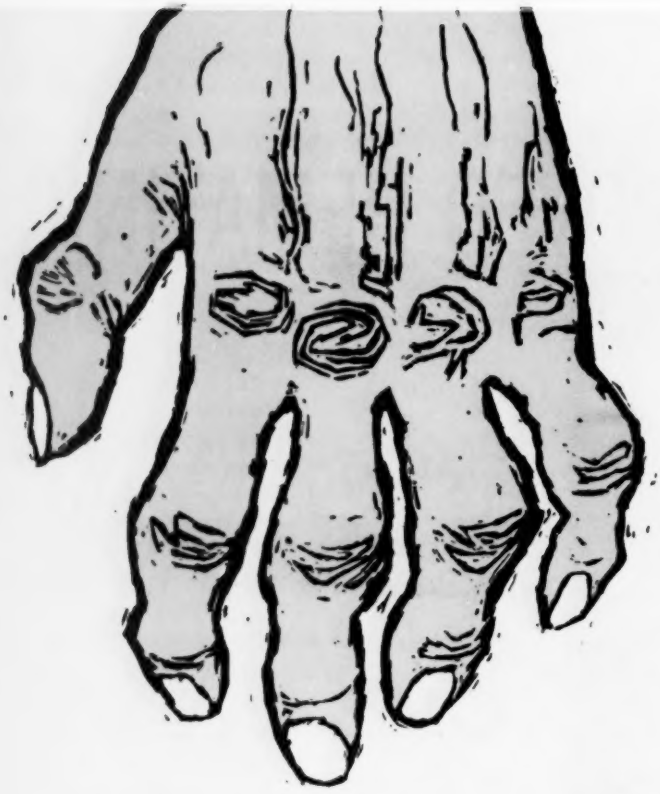

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1. Bagnall, A. W.: *Canad. M.A.J. 77*:182-194,1957.
2. Goodman, L. S., and Gilman, A.: *The Pharmacol. Basis of Therapy*, 1955, p. 299.
3. Smith, P. K., *et al.*: *J. Pharmacol. & Exper. Therap. 87*:237-255, 1946.
4. Wiggers, C. J.: *Physiol in Health & Disease*. 1955, pp. 918, 1011.

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Certain infections do not respond as well to a single agent as to a combination. *Hemophilus influenzae* infections, which are frequent in children, are a particularly serious threat to infants and children up to about 3 or 4 years of age since they have not yet built up any appreciable immunity. Serious complications such as influenzal pneumonia, empyema, or meningitis may develop, especially in this age group. In fact, except for those periods when meningococcal meningitis is epidemic, *H. influenzae* is the most frequent cause of meningitis.[1] This gram-negative organism is highly susceptible both to the tetracyclines and to the sulfonamides. Even in severe infections, therapeutic failure can be virtually eliminated by giving sulfonamides plus tetracycline.[1] These two agents together constitute the treatment of choice, and give better results than either alone.[2]

Sulfonamides remain the drugs of choice for all meningococcal infections, including meningitis. They readily penetrate the blood-brain barrier and pass into the cerebrospinal fluid in good concentrations.[3] In treating overwhelming meningococcal infections, and complicating infections of the upper respiratory tract caused by other organisms, the addition of tetracycline to sulfas can be valuable.[4]

In recent years the sulfonamides have again been prescribed more and more frequently. In certain serious infections, better results can be obtained with a combination of antibiotic and sulfonamide than with either drug alone (e.g., severe pneumococcal pneumonia or pneumococcal meningitis[5]). Furthermore, mixed infections, to which young children are particularly susceptible, often respond only to combination therapy such as tetracycline with sulfonamides (TETREX $\overline{c}$ T/S).

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References: 1. Alexander, H. E.: The hemophilus group. In: Dubois, R. J.: Bacterial and Mycotic Infections of Man. Ed. 3, Philadelphia, J. B. Lippincott Co., 1958, p. 470ff. 2. Goodman, L. S., and Gilman, A.: The Pharmacological Basis of Therapeutics. Ed. 2, New York, The Macmillan Co., 1956, pp. 1322-1323. 3. Beckman, H.: Drugs — Their Nature, Action, and Use. Philadelphia, W. B. Saunders Co., 1958, pp. 527-528. 4. Dingle, J. H.: Meningococcal infections. In: Cecil, R. L., and Loeb, R. F.: A Textbook of Medicine. Ed. 9, Philadelphia, W. B. Saunders Co., 1955, p. 196ff. 5. Goodman, L. S., and Gilman, A.: The Pharmacological Basis of Therapeutics. Ed. 2, New York, The Macmillan Co., 1956, p. 1308.

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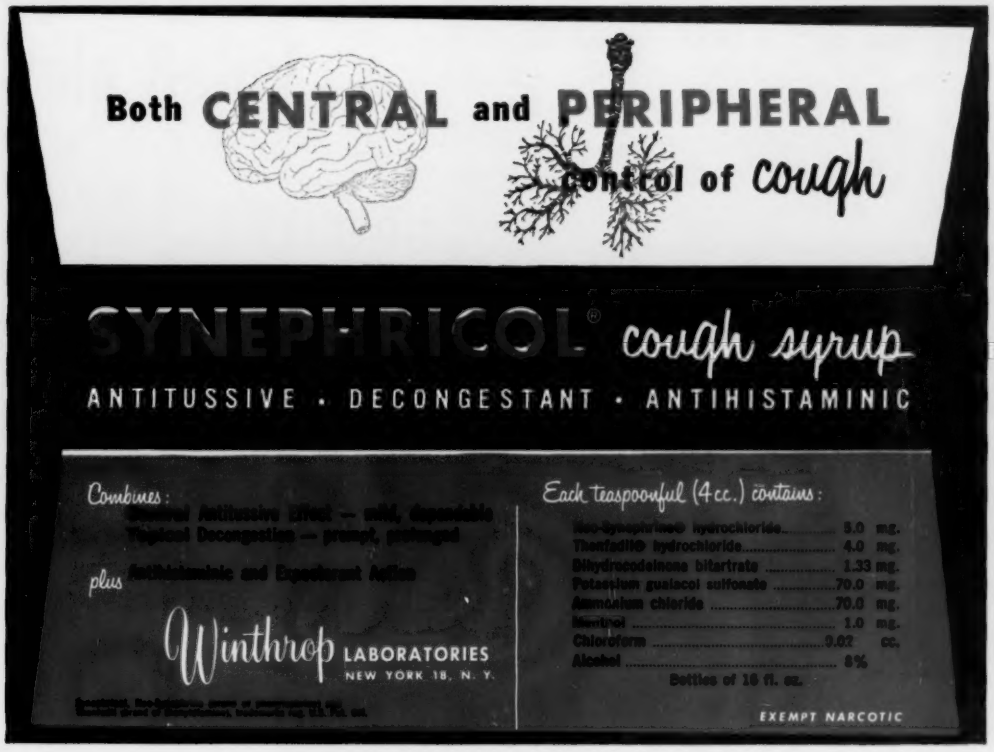

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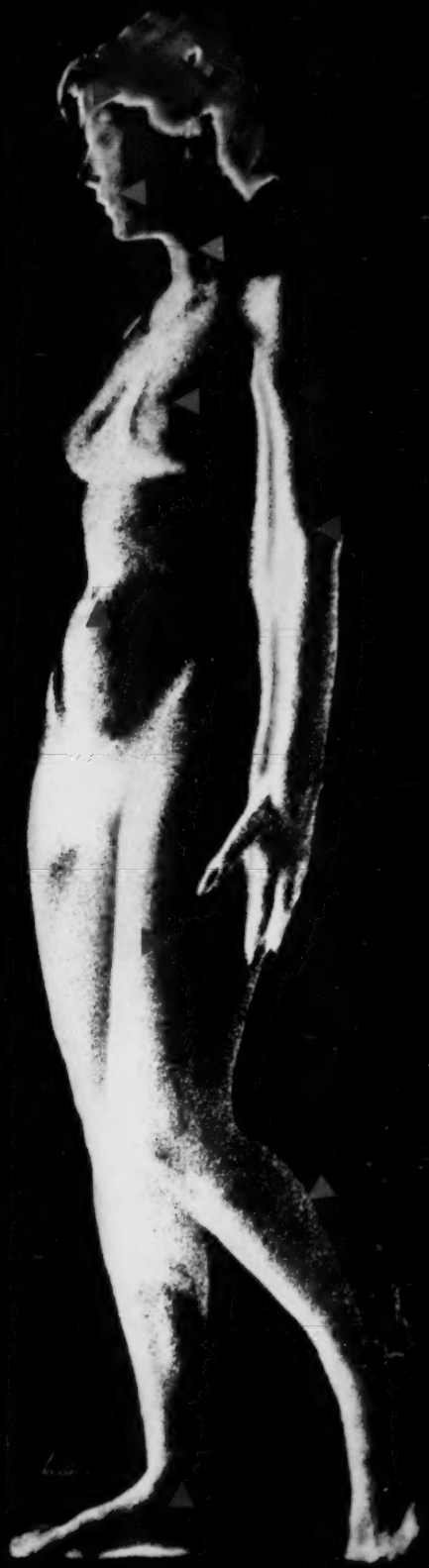

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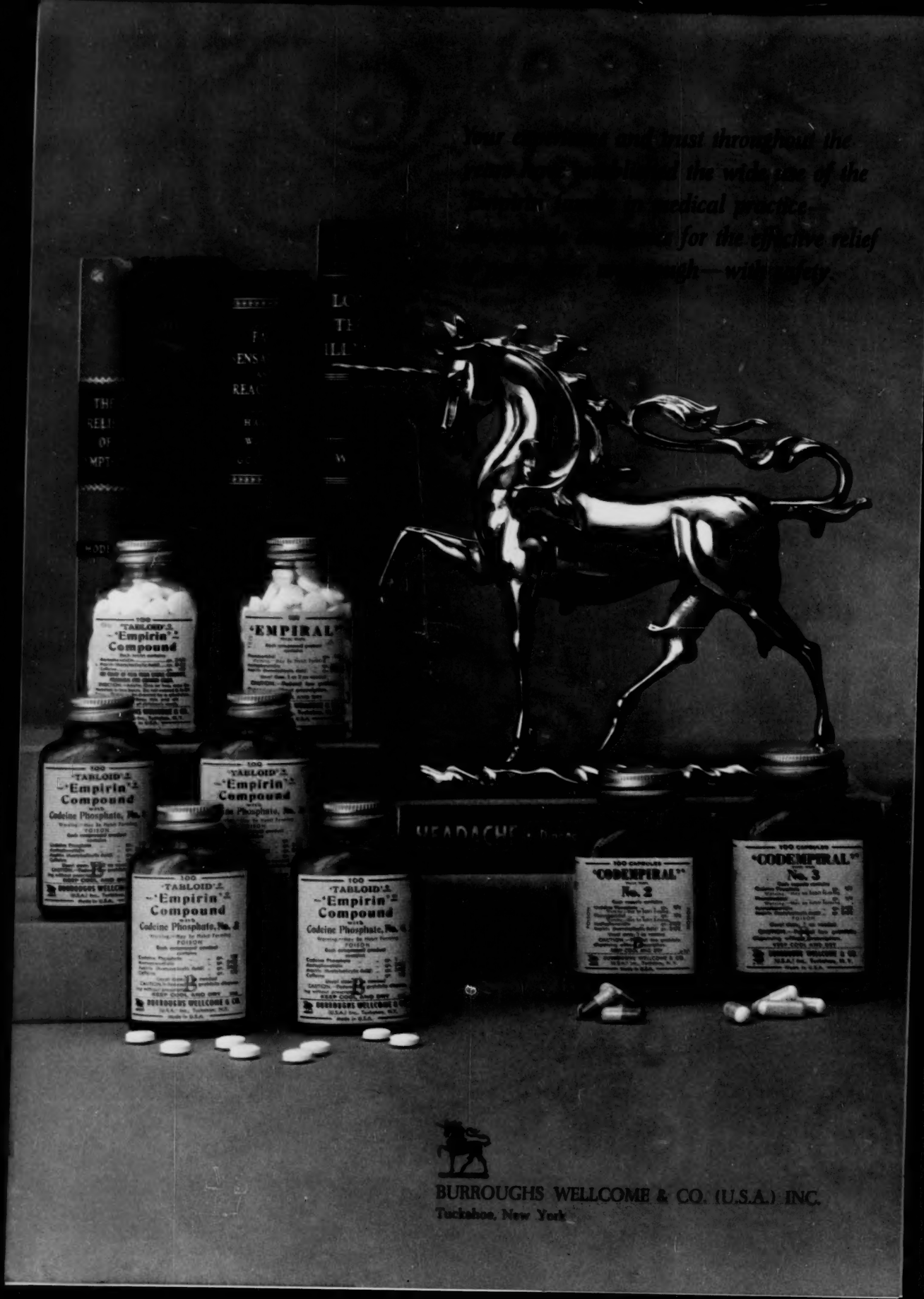

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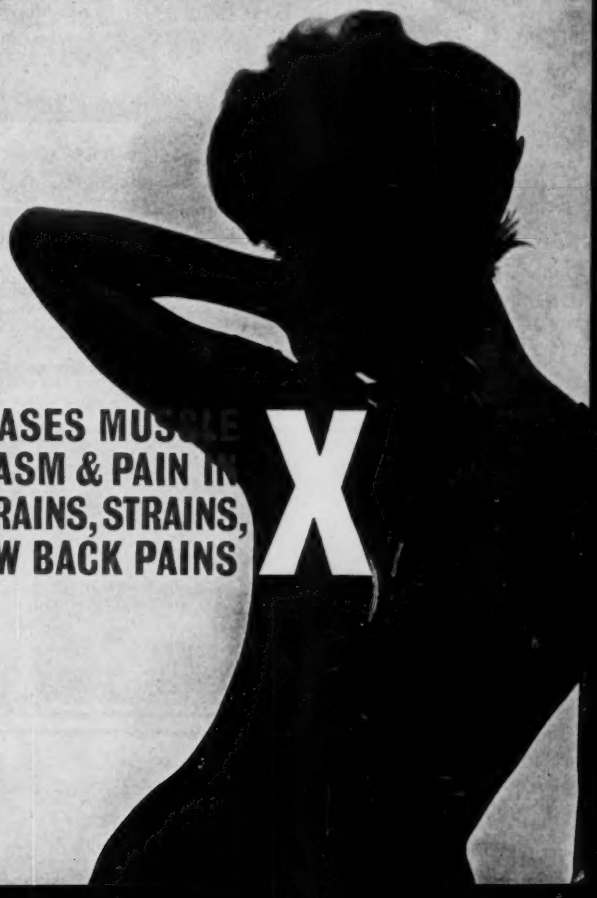

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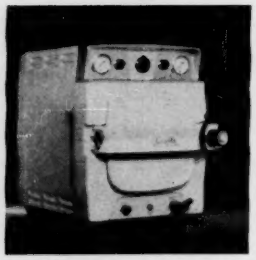

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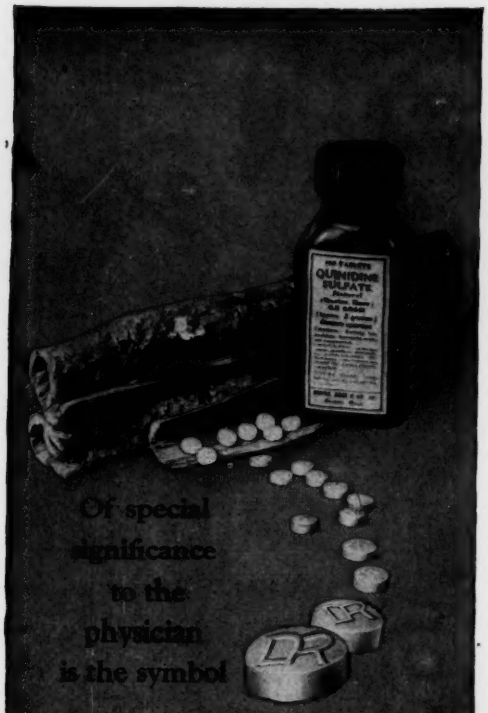

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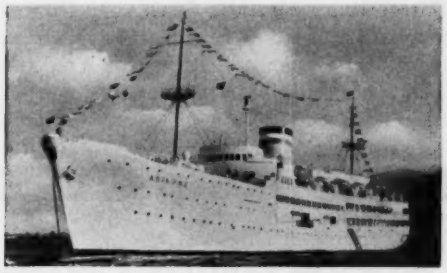

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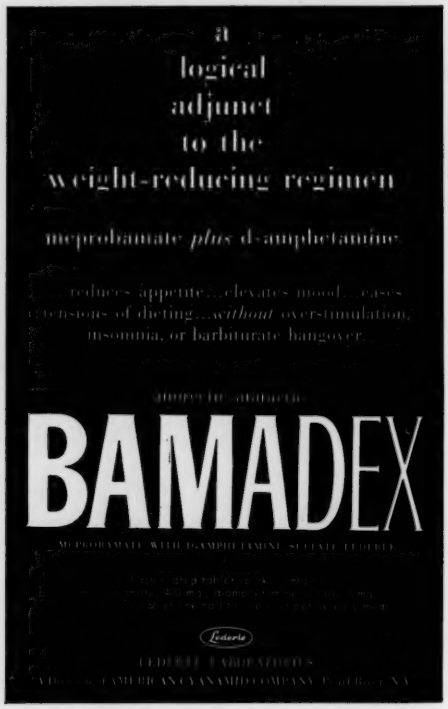

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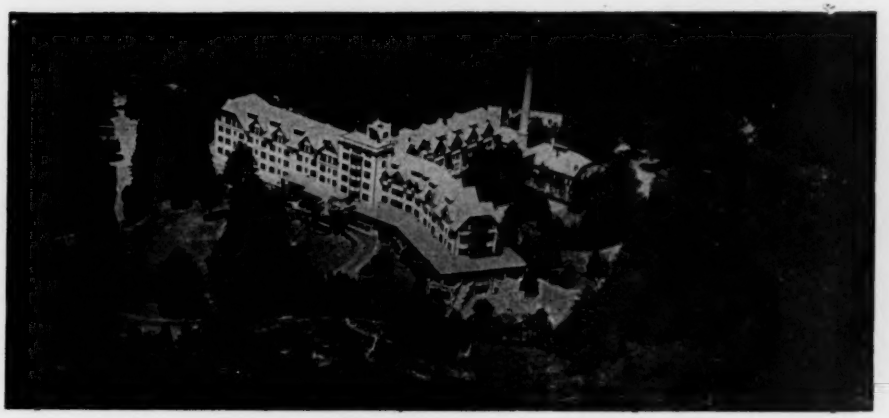

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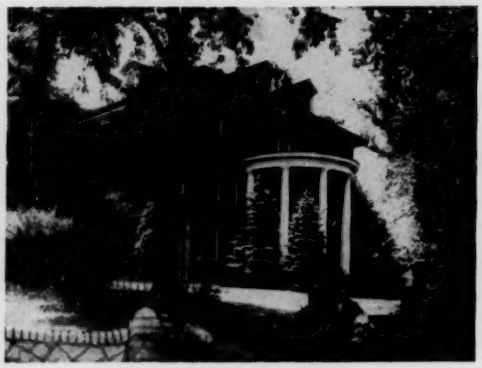

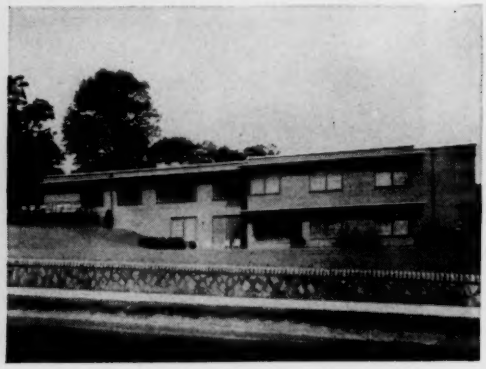

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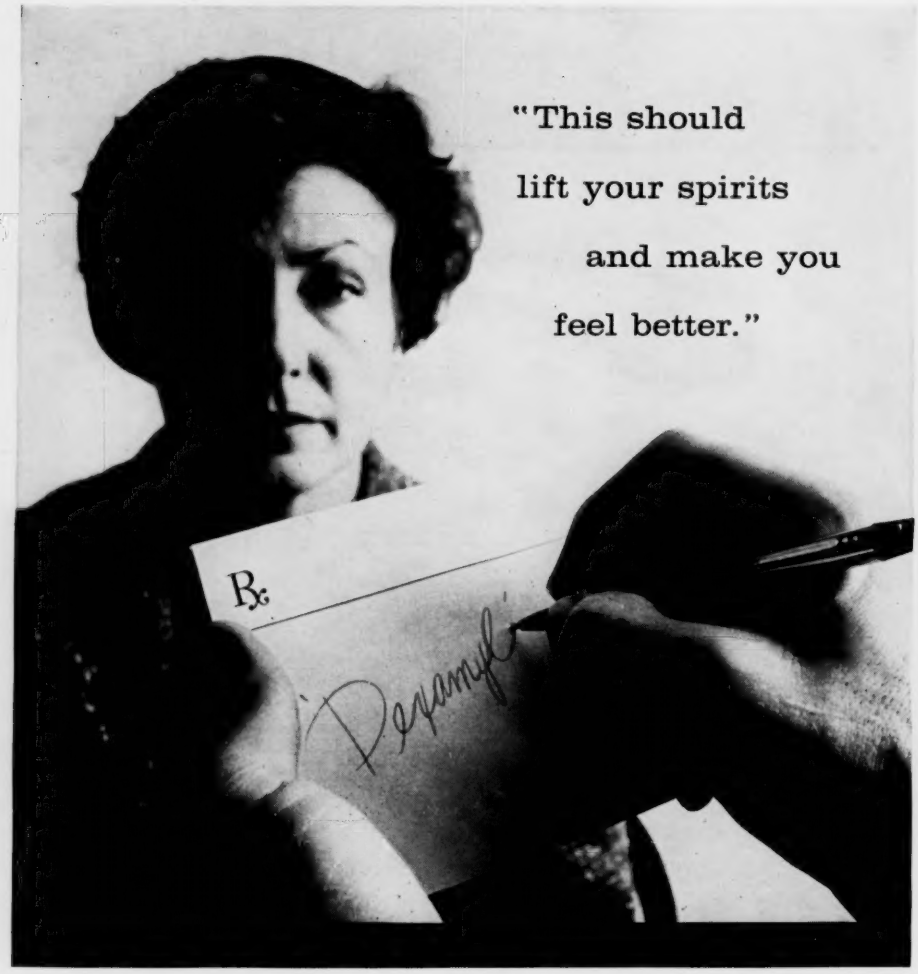

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